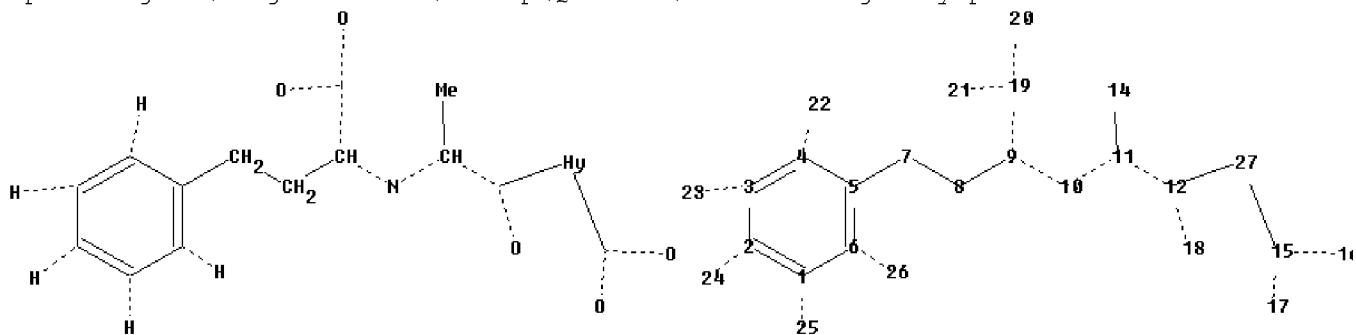


=>

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chain nodes :

7 8 9 10 11 12 14 15 16 17 18 19 20 21 22 23 24 25 26 27

ring nodes :

1 2 3 4 5 6

chain bonds :

1-25 2-24 3-23 4-22 5-7 6-26 7-8 8-9 9-10 9-19 10-11 11-12 11-14 12-18
12-27 15-17 15-16 15-27 19-20 19-21

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

1-25 2-24 3-23 4-22 6-26 9-10 9-19 10-11 11-12 12-18 12-27 15-17 15-16
15-27 19-20 19-21

exact bonds :

5-7 7-8 8-9 11-14

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:Atom

Generic attributes :

27:

Saturation : Saturated

Number of Hetero Atoms : Exactly 1

Type of Ring System : Polycyclic

L32 STRUCTURE UPLOADED

L32 STRUCTURE UPLOADED

L34 83 S L32 SSS FULL SUB=L18

FILE 'CAPLUS' ENTERED AT 10:01:13 ON 05 MAY 2008

L35 811 S L34

L36 111 S L35 AND SPN/RL

- ✓ L36 ANSWER 1 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Radioimaging moieties coupled to peptidase-binding moieties for imaging tissues and organs that express peptidases
- ✓ L36 ANSWER 2 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Methods and compositions of gene delivery to epithelial cells through bile acid peptide conjugate delivery agents for systemic and local therapy
- ✓ L36 ANSWER 3 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of pyrrolopyrimidines having MnK1/MnK2 inhibiting activity
- ✓ L36 ANSWER 4 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of 1-heterocyclylamino-2-hydroxy-3-amino- ω -arylalkanes as renin inhibitors for treating hypertension and other renin-mediated diseases
- ✓ L36 ANSWER 5 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ 6-(Aminoalkyl)indazoles as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with renin activity
- ✓ L36 ANSWER 6 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Acylpiperidine compounds as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with aspartic protease activity
- ✓ L36 ANSWER 7 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Piperidinyl pyrrolidinyl methanone compounds as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with aspartic protease activity
- ✓ L36 ANSWER 8 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Thienopyrimidines having MnK1/MnK2 inhibiting activity for pharmaceutical compositions

- √ L36 ANSWER 9 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Piperidines and morpholines as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with renin activity
- √ L36 ANSWER 10 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Preparation of substituted thiazolopyridines as PPAR modulators
- √ L36 ANSWER 11 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Preparation of substituted thiazolyl tetrahydroisoquinolines as PPAR modulators
- √ L36 ANSWER 12 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Spiro imidazole derivatives as PPAR modulators and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with PPAR activity.
- √ L36 ANSWER 13 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- √ L36 ANSWER 14 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- √ L36 ANSWER 15 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- √ L36 ANSWER 16 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Combination of a dipeptidyl peptidase-4 inhibitor and an anti-hypertensive agent for the treatment of diabetes and hypertension
- √ L36 ANSWER 17 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:397799 CAPLUS Full-text
DN 147:212296
TI Improved process for preparation of trandolapril
IN Dattatraya, Patil Vishvas; Sharadrao, Varangaonkar Aniruddha
PA Torrent Pharmaceuticals Ltd., India

SO Indian Pat. Appl., 19pp.

CODEN: INXXBQ

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|----------------|------|----------|-----------------|----------|
| PI | IN 2004KO00355 | A | 20060825 | IN 2004-KO355 | 20040625 |

PRAI IN 2004-KO355

OS CASREACT 147:212296

AB The invention discloses an improved process for the preparation of (2S,3aR,7aS)-1-[N-[(S)-1-carbethoxy-3-phenylpropyl]-L-alanyl]hexahydro-2-indolinecarboxylic acid, i.e., trandolapril. Key steps in the process include treating Me 3-chloro-N-acetylalanine with 1-pyrrolidinocyclohexene, followed by hydrolysis with 2N HCl and reductive cyclization over Pt/C to obtain 2 β ,3a β ,7a α -1H-octahydroindole-2-carboxylic acid hydrochloride. The N-benzoyl derivative was resolved via formation of the L- α -phenylethylamine salt.

IT 87679-37-6P, Trandolapril

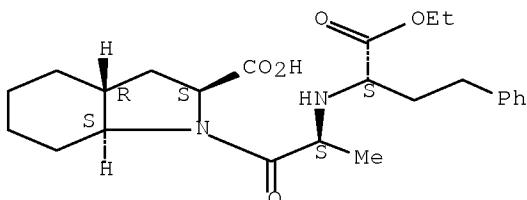
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(improved process for preparation of trandolapril)

RN 87679-37-6 CAPPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 98677-37-3P

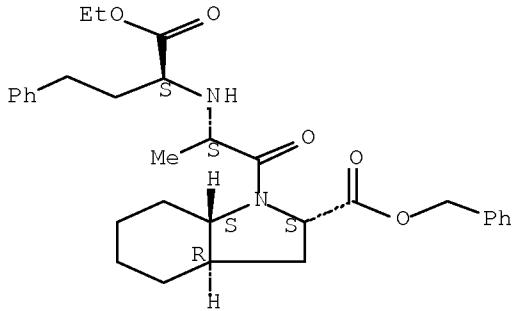
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(improved process for preparation of trandolapril)

RN 98677-37-3 CAPPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



√ L36 ANSWER 18 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:388837 CAPLUS Full-text
 DN 147:541727
 TI Process for the preparation of trandolapril and intermediates thereof
 IN Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Ramam, Buddhavarapu
 Pattabhi; Bodkhe, Arjun Rajaram
 PA Glenmark Pharmaceuticals Limited, India
 SO Indian Pat. Appl., 31pp.
 CODEN: INXXBQ
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---------------------|------|------------|-----------------|----------|
| PI | IN 2004MU01060 | A | √ 20060728 | IN 2004-MU1060 | 20041007 |
| PRAI | IN 2004-MU1060 | | 20041007 | | |
| OS | CASREACT 147:541727 | | | | |
| GI | | | | | |

L36 ANSWER 19 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:300486 CAPLUS Full-text
 DN 147:522095
 TI Process for the preparation of trans-octahydro-1H-indole-2-carboxylic acid
 IN Debasish, Datta; Jagannath, Wani Mukesh
 PA Lupin Ltd., India
 SO Indian Pat. Appl., 37pp.
 CODEN: INXXBQ
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---------------------|------|----------|-----------------|----------|
| PI | IN 2003MU01033 | A | 20060120 | IN 2003-MU1033 | 20031003 |
| PRAI | IN 2003-MU1033 | | 20031003 | | |
| OS | CASREACT 147:522095 | | | | |
| GI | | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a process for the preparation of octahydroindole-2-carboxylic acid of formula I, wherein the ring junction is trans, including enantiomers, esters, and salts thereof, and more specifically (2S, 3aR, 7aS)-octahydro-1H-indole-2-carboxylic acid (II) and esters and salts thereof. Compound II is a valuable intermediate in the synthesis of the angiotensin converting enzyme (ACE) inhibitor trandolapril. The process of the invention avoids the use of expensive, hazardous, toxic, and corrosive chems., very low temps., and gives about 50% of the trans-isomer, making the process of the invention more com. attractive than prior art. The target compds. may be prepared according to the process of the invention as shown by the following example. Rhodium-catalyzed hydrogenation of the hydrochloride of imino acid III in water under alkaline conditions gave about 1:1 mixture of the trans- and cis-isomers of I. Fractional crystallization of the mixture from methanol resulted in the isolation of II and its enantiomer. Acetylation followed by diastereomeric salt formation with cinchonidine and acidification gave IV with 99.7% optical purity. Compound IV underwent deacetylation with hydrochloric acid to give II, which may be used to prepare trandolapril (V) in a single step.

IT 87679-37-6P, Trandolapril

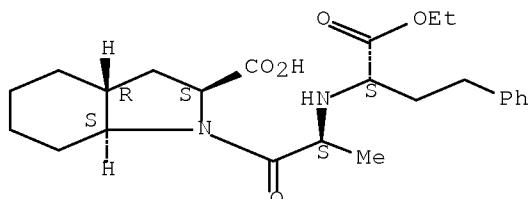
RL: IMF (Industrial manufacture); SPN (Synthetic preparation);
PREP (Preparation)

(target compound; process for preparation of trans-octahydro-1H-indole-2-carboxylic acid)

RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



√ L36 ANSWER 20 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI √ Nitric oxide enhancing angiotensin II antagonist compounds, and their preparation, compositions, and methods of use

√ L36 ANSWER 21 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:37921 CAPLUS Full-text

DN 146:143003

TI Process for the preparation of trandolapril from N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine N-carboxyanhydride and trans-octahydro-1H-indole-2-carboxylic acid.

IN Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra; Phull, Manjinder

PA Singh; Sawant, Ashwini; Birari, Dilip Ramdas
Cipla Limited, India; Curtis, Philip, Anthony
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|--|----------|-----------------|----------|
| PI | WO 2007003947 | A2 | 20070111 | WO 2006-GB2496 | 20060705 |
| | WO 2007003947 | A3 | 20070531 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | |
| | IN 2005MU00793 | A | 20070601 | IN 2005-MU793 | 20050705 |
| | CA 2614099 | A1 | 20070111 | CA 2006-2614099 | 20060705 |
| | EP 1899300 | A2 | 20080319 | EP 2006-755717 | 20060705 |
| | R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | |
| PRAI | IN 2005-MU793 | A | ✓ | 20050705 | |
| | WO 2006-GB2496 | W | | 20060705 | |

√ L36 ANSWER 22 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Thienopyrimidines for pharmaceutical compositions and their preparation
and use as kinase inhibitors

L36 ANSWER 23 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:1339720 CAPLUS Full-text
DN 146:82189
TI Preparation of L-threonine derivatives with high therapeutic index
IN Chandran, V. Ravi
PA USA
SO U.S. Pat. Appl. Publ., 60pp., Cont.-in-part of U.S. Ser. No. 343,557.
CODEN: USXXCO

DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|----------------|---|----------|-----------------|----------|
| PI | US 20060287244 | A1 | 20061221 | US 2006-442027 | 20060526 |
| | WO 2005046575 | A2 | 20050526 | WO 2004-US24901 | 20040729 |
| | WO 2005046575 | A3 | 20071004 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, | | | |

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG, AP, EA, EP, OA
 US 20060241017 A1 20061026 US 2006-343557 20060130
 PRAI US 2003-491331P P 20030729
 WO 2004-US24901 A2 20040729
 US 2006-343557 A2 20060130

AB The invention is directed to novel therapeutic compds. comprised of an L-threonine bonded to a medicament or drug having a hydroxy, amino, carboxy or acylating function. These high-therapeutic index derivs. have the same utility as the drug from which they are made and they have enhanced pharmacol. and pharmaceutical properties, with the addnl. advantage of separating various enantiomeric and diastereomeric drugs into their individual isomers. The examples describe the synthesis and activities of L-threonine derivs. of (\pm)- and (+)-(S)-ibuprofen, (\pm)- and (+)-(S)-ketoprofen, (-)-(S)-ketorolac, aspirin, and fenofibric acid. The synthesis and activity of several L-serine and L-hydroxypyroline analogs were also described. Thus, the hydrochloride of (+)-(S)-ibuprofen ester of L-threonine was prepared, and its free base examined for analgesic, gastric mucosal irritation, toxicity, and pharmacokinetic properties.

IT 917472-72-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of L-threonine derivs. with high therapeutic index)

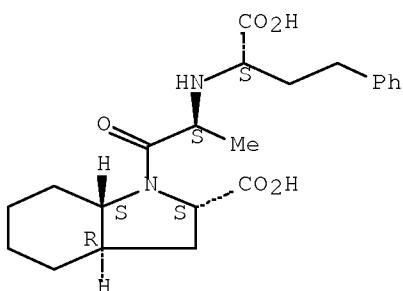
RN 917472-72-1 CAPLUS

CN L-Threonine, ester with (2S,3aR,7aS)-1-[(2S)-2-[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (CA INDEX NAME)

CM 1

CRN 87679-71-8
CMF C22 H30 N2 O5

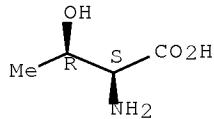
Absolute stereochemistry.



CM 2

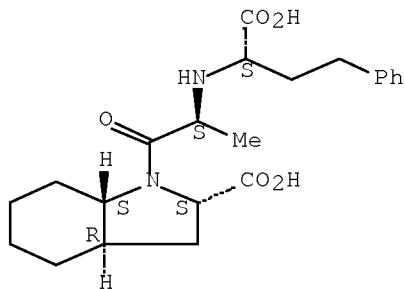
CRN 72-19-5
CMF C4 H9 N O3

Absolute stereochemistry.



IT 87679-71-8, Trandolaprilat
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of L-threonine derivs. with high therapeutic index)
RN 87679-71-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



✓ L36 ANSWER 24 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of pyrazole compounds as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes

✓ L36 ANSWER 25 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of 4-biaryl-1-phenylazetidin-2-ones for the treatment of hypercholesterolemia

✓ L36 ANSWER 26 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1222092 CAPLUS Full-text
DN 146:7821
TI Process for the preparation of (2S,3aR,7aS)-octahydroindole-2-carboxylates and their conversion to trandolapril
IN Akhtar, Haider; Ramesh, Babu Potluri; Venkata, Subhramanian

PA Hariharakrishnan; Hari, Prassad Kodali
Sochinaz SA, Switz.
SO Eur. Pat. Appl., 19pp.

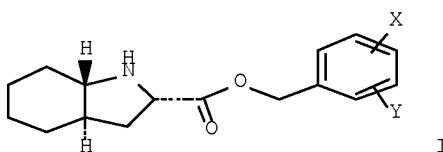
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|------------|-----------------|----------|
| PI | EP 1724260 | A1 | ✓ 20061122 | EP 2005-76060 | 20050506 |
| | EP 1724260 | B1 | 20080220 | | |
| | R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU | | | | |
| | AT 386718 | T | 20080315 | AT 2005-76060 | 20050506 |
| PRAI | EP 2005-76060 | A | 20050506 | | |
| OS | CASREACT 146:7821; MARPAT 146:7821 | | | | |
| GI | | | | | |



AB A process for preparation of benzyl (2S,3aR,7aS)-octahydroindole-2-carboxylate hydrohalide (I; X, Y = H, halo, alkyl, alkoxy), and its conversion to trandolapril comprises (a) reaction of Me β -hydroxyalaninate hydrochloride with an acylating agent in a nonpolar solvent to give a diacylated derivative, (b) reaction of the latter with a cyclohexanone enamine to give Me N-acyl- β -(2-oxocyclohexyl)alaninate, (c) hydrolytic cyclization to give an indole, (d) hydrogenation to a perhydroindole derivative, (e) esterification with a benzyl alc. followed by conversion of the benzyl ester arylsulfonate to the hydrohalide I, (f) resolution and conversion to a benzyl (2S,3aR,7aS)-octahydroindole-2-carboxylate hydrohalide, and (g) coupling with ECPA (N-[(1-ethoxycarbonyl)-3- phenylpropyl]-(S)-alanine) acid chloride hydrochloride and debenzylating hydrogenolysis.

✓ L36 ANSWER 27 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI ✓ 4-Biaryl-1-phenylazetidin-2-one glucuronide derivatives for hypercholesterolemia

L36 ANSWER 28 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:1124123 CAPLUS Full-text

DN 145:455276

TI Preparation of amino acid derivatives with high therapeutic index

IN Chandran, V. Ravi

PA USA

SO U.S. Pat. Appl. Publ., 139pp.

CODEN: USXXCO

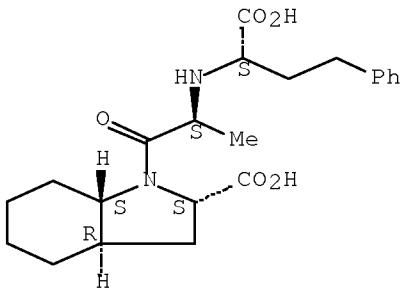
DT Patent

LA English

FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|----------|
| PI | US 20060241017 | A1 | 20061026 | US 2006-343557 | 20060130 |
| | WO 2005046575 | A2 | 20050526 | WO 2004-US24901 | 20040729 |
| | WO 2005046575 | A3 | 20071004 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA | | | | |
| | US 20060287244 | A1 | 20061221 | US 2006-442027 | 20060526 |
| | WO 2007089745 | A2 | 20070809 | WO 2007-US2475 | 20070129 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| PRAI | US 2003-491331P | P | 20030729 | | |
| | WO 2004-US24901 | A2 | 20040729 | | |
| | US 2006-343557 | A2 | 20060130 | | |
| AB | The invention is directed to novel therapeutic compds. comprised of an amino acid bonded to a medicament or drug having a hydroxy, amino, carboxy or acylating function. These high-therapeutic index derivs. have the same utility as the drug from which they are made and they have enhanced pharmacol. and pharmaceutical properties. The examples describe the synthesis and activities of amino acid derivs. of propofol, ibuprofen, ketoprofen, ketorolac, aspirin, acetaminophen, cyclosporin A, valproic acid, clopidogrel, damazol, benzapril, enalapril, and fenofibric acid. Thus, (\pm)-ibuprofen esters of L-serine, L-threonine, and L-hydroxyproline were prepared and examined for analgesic, gastric mucosal irritation, toxicity, and pharmacokinetic properties. | | | | |
| IT | 87679-71-8, Trandolaprilat | | | | |
| | RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses) | | | | |
| | (preparation of amino acid derivs. with high therapeutic index) | | | | |
| RN | 87679-71-8 CAPLUS | | | | |
| CN | 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- | | | (CA INDEX NAME) | |

Absolute stereochemistry.



✓ L36 ANSWER 29 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 TI ✓ Organic nitric oxide enhancing salts of angiotensin II antagonists, compositions and methods of use

✓ L36 ANSWER 30 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 TI ✓ Preparation of nitric oxide enhancing diuretic compounds, compositions and methods of use

✓ L36 ANSWER 31 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:818063 CAPLUS Full-text
 DN 145:211348
 TI Improved process for preparation of highly pure trandolapril
 IN Singh, Girij Pal; Wani, Mukesh Jagannath; Lande, Hemraj Mahadeorao; Jain, Adinath Murlidhar
 PA Lupin Limited, India
 SO PCT Int. Appl., 34pp.

CODEN: PIXXD2

DT Patent

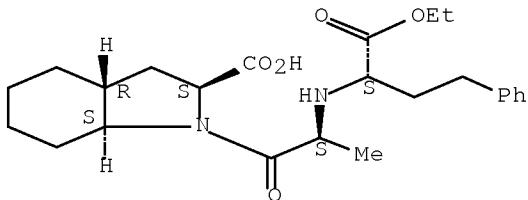
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----|--|------|----------|-----------------|------------|
| PI | WO 2006085332 | A1 | 20060817 | WO 2005-IN301 | ✓ 20050906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, | | | | |

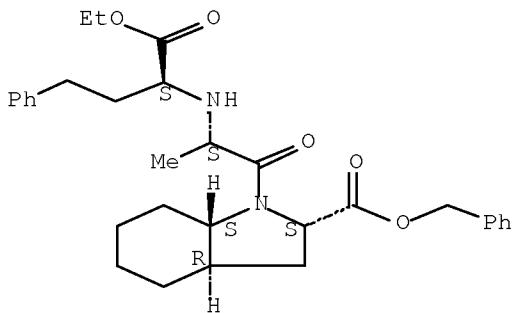
KG, KZ, MD, RU, TJ, TM
 IN 2005MU00155 A 20060908 IN 2005-MU155 20050214
 AU 2005327440 A1 20060817 AU 2005-327440 20050906
 EP 1866327 A1 20071219 EP 2005-823818 20050906
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
 PRAI IN 2005-MU155 A 20050214
 WO 2005-IN301 W 20050906
 OS CASREACT 145:211348
 AB Highly pure trandolapril was prepared by acylation of benzyl trans-(2S,3aR,7aS)-octahydro-1H-indolecarboxylate [(2S,3aR,7a)-I] with N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine N-carboxyanhydride, followed by crystallization from appropriate solvents. (2S,3aR,7a)-I was prepared by (1) crystallization of a mixture of racemic I tosylates (2S,3aR,7aS and 2R,3aS,7aR) to enrich the purity to >99% from a mixture containing the cis diastereomers up to 6 %, (2) optical resolution of the racemic mixture of (2S,3aR,7aS)- and (2R,3aS,7aR)-I with (-)-dibenzoyl-L-tartaric acid monohydrate, (3) reaction of the tartrate salt with N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine N-carboxyanhydride to give trandolapril benzyl ester, and crystallization of crude trandolapril. Trandolapril obtained by this process had HPLC purity 99.94% and a characteristic X-ray powder diffraction pattern.
 IT 87679-37-6P, Trandolapril
 RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
 (X-ray powder diffraction; preparation of highly pure trandolapril)
 RN 87679-37-6 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 98677-37-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of highly pure trandolapril)
 RN 98677-37-3 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
 (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ L36 ANSWER 32 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Hydroxylated nebivolol metabolites for treating and/or preventing
vascular
diseases

✓ L36 ANSWER 33 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ 1-Acylamino-2-hydroxy-3-amino-w-arylalkanes as renin inhibitors and
their
preparation, pharmaceutical compositions and their use for treatment of
hypertension

✓ L36 ANSWER 34 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of 4-
[(benzimidazolyl/pyrazolyl/triazolyl)methoxy]phenoxyacetic
acids as PPAR modulators

✓ L36 ANSWER 35 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of pyrazolopyrimidines as inhibitors of kinase activity

✓ L36 ANSWER 36 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Diuretic compounds comprising heterocyclic nitric oxide donor groups,
compositions and methods of use

✓ L36 ANSWER 37 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Nitrosated and nitrosylated compounds, compositions, and methods for

the
treatment of ophthalmic disorders

✓ L36 ANSWER 38 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:341506 CAPLUS Full-text
DN 144:350983
TI Process for the preparation of (2S,3aR,7aS)-perhydroindole-2-carboxylic acid intermediate in synthesis of trandolapril
IN Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Ramam, Buddhavarapu Pattabhi; Bodkhe, Arjun Rajaram
PA Glenmark Pharmaceuticals Limited, India
SO U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

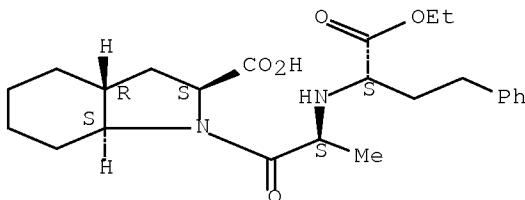
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|------------|-----------------|----------|
| PI US 20060079698 | A1 | 20060413 | US 2005-245871 | 20051007 |
| PRAI US 2004-616934P | P | ✓ 20041007 | | |
| US 2004-616959P | P | 20041007 | | |
| OS CASREACT 144:350983; MARPAT 144:350983 | | | | |

AB Trandolapril intermediate (2S,3aR,7aS)-perhydroindole-2-carboxylic acid was prepared by a process which comprises esterification of (3aR,7aS)-perhydroindole-2-carboxylic acid with an alc. in the presence of an acid, reacting the acid addition salt with a base and then dibenzoyl-L-tartaric acid or di-p-toluoyl-L-tartaric acid and at least one alc., followed by addition of a second base and hydrolysis. (2S,3aR,7aS)-perhydroindole-2-carboxylic acid prepared by this method was used to prepare trandolapril.

IT 87679-37-6P, Trandolapril
RL: IMF (Industrial manufacture); SPN (Synthetic preparation);
PREP (Preparation)
(preparation of perhydroindolecarboxylic acid intermediate in synthesis of trandolapril)

RN 87679-37-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



✓ L36 ANSWER 39 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of bicyclic anilide spirolactam cgrp receptor antagonists

√ L36 ANSWER 40 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Preparation of tricyclic anilide spirohydantoin CGRP receptor antagonists

√ L36 ANSWER 41 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:119252 CAPLUS Full-text
DN 144:171268
TI Preparation of trandolapril
IN Reddy, Pratap Padi; Chitre, Saurabh Shashikant; Polavarapu, Srinivas;
Vakamudi Sri Naga Venkata Laxmi, Varaprasad
PA Dr. Reddy's Laboratories Ltd., India; Dr. Reddy's Laboratories, Inc.
SO PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DT Patent

LA English

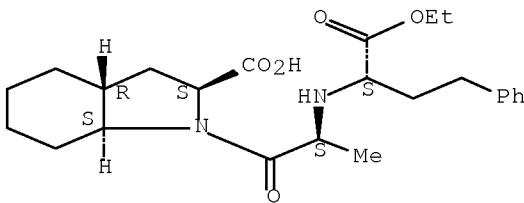
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|------------|-----------------|----------|
| PI | WO 2006014916 | A2 | 20060209 | WO 2005-US26423 | 20050726 |
| | WO 2006014916 | A3 | 20060803 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | IN 2007CN00572 | A | 20070824 | IN 2007-CN572 | 20070208 |
| PRAI | US 2004-591035P | P | √ 20040726 | | |
| | US 2004-607839P | P | 20040908 | | |
| | WO 2005-US26423 | W | 20050726 | | |
| OS | CASREACT 144:171268 | | | | |
| AB | The invention relates to a process for preparing trandolapril, (2S,3aR,7aS)-1-[N-[(S)-1-carbethoxy-3-phenylpropyl]-L-alanyl]hexahydro-2-indolecarboxylic acid, and intermediates formed in the process. Thus, (±)-benzyl octahydro-2-indolecarboxylate hydrochloride was treated with N-[(S)-1-carbethoxy-3-phenylpropyl]-L-alanine in CH ₂ C ₁₂ in the presence of hydroxybenzotriazole and dicyclohexylcarbodiimide at 20–25°C for 3 h. Hydrogenation over 10% Pd on charcoal and workup, including recrystn., afforded trandolapril. | | | | |

√ L36 ANSWER 42 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Thiazole compounds as PPAR modulators, their preparation, pharmaceutical

compositions, and use in therapy

- ✓ L36 ANSWER 43 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Oxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- ✓ L36 ANSWER 44 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Triaryl compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- ✓ L36 ANSWER 45 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Isoxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- ✓ L36 ANSWER 46 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Combination of (S)-amlodipine and an ACE inhibitor for reducing hypertension
- ✓ L36 ANSWER 47 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of diacylglycerol acyltransferase (DGAT1) inhibitors as anorectics.
- ✓ L36 ANSWER 48 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Nitric oxide-releasing pyruvate compounds, compositions and methods for treating cardiovascular and other diseases
- ✓ L36 ANSWER 49 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN - INSTANT
- | | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|------|----------|-----------------|----------|
| PI | WO 2005054194 | A1 | 20050616 | WO 2004-EP13377 | 20041125 |
| | US 20070225505 | A1 | 20070927 | US 2007-580610 | 20070212 |
| PRAI | EP 2003-257417 | A | 20031125 | | |
| | WO 2004-EP13377 | W | 20041125 | | |



✓ L36 ANSWER 50 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:493585 CAPLUS Full-text
 DN 143:32341
 TI Method for producing {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid} compounds especially trandolapril via their racemic salts
 IN Pogutter, Mirko; Rudolf, Felix; Bichsel, Hans-Ulrich; Bader, Thomas
 PA Azad Pharmaceuticals Ingredients A.-G., Switz.
 SO PCT Int. Appl., 37 pp.
 CODEN: PIXXD2
 DT Patent
 LA German
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|------------|
| PI | WO 2005051909 | A1 | 20050609 | WO 2004-CH688 | ✓ 20041115 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1689711 | A1 | 20060816 | EP 2004-797245 | 20041115 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | |
| | JP 2007512260 | T | 20070517 | JP 2006-540130 | 20041115 |
| | IN 2006KN01385 | A | 20070504 | IN 2006-KN1385 | 20060523 |
| | US 20070135513 | A1 | 20070614 | US 2007-580638 | 20070208 |
| PRAI | CH 2003-2038 | A | 20031128 | | |
| | WO 2004-CH688 | W | 20041115 | | |
| AB | The invention relates to a method for producing optionally substituted {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid} and the pharmaceutically acceptable salts thereof. To this end, a racemic mixture of optionally substituted trans-octahydroindol-2-carboxylic acid is reacted with the N-carboxyanhydride of {N-[1-(S)-alkoxycarbonyl-3-phenylpropyl]-L-alanine}, which is optionally substituted on the Ph ring, in an appropriate inert solvent, and the obtained optionally substituted {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid}, preferably trandolapril, is subsequently isolated, as well as polymorphous forms A and B of trandolapril. | | | | |

- ✓ L36 ANSWER 51 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of nitrosated glutamic acid compounds for use in pharmaceutical compositions
- ✓ L36 ANSWER 52 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of biphenyl or phenylheterocyclyl moiety-containing esters as inhibitors of microsomal triglyceride transfer protein
- ✓ L36 ANSWER 53 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ 2'-Benzothiazolylthioesters of N-substituted alpha amino acids: versatile intermediates for synthesis of ACE inhibitors
SO ✓ Synthetic Communications (2005), 35(2), 243-248
- ✓ L36 ANSWER 54 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Nitrosated and nitrosylated cardiovascular compounds, their compositions, and use
- ✓ L36 ANSWER 55 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of benzodiazepine derivatives as CGRP receptor antagonists
- ✓ L36 ANSWER 56 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive and anticancer agents
- ✓ L36 ANSWER 57 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases
- ✓ L36 ANSWER 58 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of α -amino acid benzothiazolylthio esters as intermediates for manufacture of ACE inhibitors

√ L36 ANSWER 59 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Preparation of benzodiazepine CGRP receptor antagonists

√ L36 ANSWER 60 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Enalapril-nitroxy derivatives and related compounds as ace inhibitors
for the treatment of cardiovascular diseases

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------|------|----------|-----------------|----------|
| PI WO 2004110432 | A1 | 20041223 | WO 2004-EP51089 | 20040611 |
| PRAI EP 2003-101796 | A | 20030619 | | |
| WO 2004-EP51089 | W | √ | 20040611 | |

√ L36 ANSWER 61 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI Process for the preparation of enalapril maleate and related compounds
having ACE inhibitory action

IN Jenko, Branko
PA Lek Pharmaceuticals D.D., Slovenia
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| PI WO 2004101515 | A1 | 20041125 | WO 2004-SI21 | √ 20040507 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| SI 21507 | A | 20041231 | SI 2003-123 | 20030516 |
| EP 1628956 | A1 | 20060301 | EP 2004-731808 | 20040507 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| US 20070072919 | A1 | 20070329 | US 2006-556986 | 20060929 |
| PRAI SI 2003-123 | A | 20030516 | | |
| WO 2004-SI21 | W | 20040507 | | |

√ L36 ANSWER 62 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:931415 CAPLUS Full-text

DN 141:366125
TI Preparation of trandolapril from diastereomeric salt of benzyl (2S,3aR,7aS)-hexahydro-2-indolinecarboxylate
IN Shimamura, Hiroshi
PA Ohara Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------------------|------|------------|-----------------|----------|
| PI JP 2004307340 | A | ✓ 20041104 | JP 2003-73056 | 20030318 |
| PRAI JP 2003-37749 | A | 20030217 | | |

AB Trandolapril (I) is prepared by amidation of benzyl (2S,3aR,7aS)-hexahydro-2-indolinecarboxylate (II) salt with optically active 10-camphorsulfonic acid, with N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine or its N-carboxyanhydride (III) in tertiary amine-containing solvent, followed by hydrogenolysis of the resulting amide benzyl ester. Thus, II.(1R)-(-)-10-camphorsulfonate was amidated with III in DMF in the presence of Et₃N, then hydrogenated over Pd/C to give I with 82% total yield.

✓ L36 ANSWER 63 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of azole compounds as PTP1B inhibitors

✓ L36 ANSWER 64 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Evaluation of adsorption and penetration of angiotensin converting enzyme inhibitor, trandolapril, and its active metabolite, trandolaprilate, to the dialysis membrane
AU Zaitsu, Kiyoshi; Hamase, Kenji; Hayashi, Hiromi; Nagayasu, Reiko; Fukuda, Hiroko; Tomita, Tatsunosuke; Morikawa, Akiko
CS Graduate School of Pharmaceutical Sciences, Kyushu University, Japan
SO ✓ Igaku to Yakugaku (2004), 51(6), 843-849
CODEN: IGYAEI; ISSN: 0389-3898

✓ L36 ANSWER 65 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN - CHECKED DOC
TI Novel crystalline forms of trandolapril

✓ L36 ANSWER 66 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:633914 CAPLUS Full-text
DN 141:140316
TI Process for producing intermediate for trandolapril by esterification of racemic (2S,3aR,7aS)-hexahydroindoline-2-carboxylic acid with benzyl alcohol and optical resolution
IN Shimamura, Hiroshi; Nakata, Yoshitaka

PA Ohara Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|------------|--|----------|
| PI | WO 2004065368 | A1 | ✓ 20040805 | WO 2004-JP374 | 20040119 |
| | | | | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ | |

✓ L36 ANSWER 67 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:605707 CAPLUS Full-text
DN 141:117164
TI Preparation of (2S,3aR,7aS)-1-[(S)-N-[(S)-1-ethoxycarbonyl-3-phenylpropyl]alanyl]hexahydro-2-indolinecarbon acid benzyl ester as an antihypertensive agent
IN Shimamura, Hiroshi
PA Ohara Yakuhin Kogyo K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|------------|-----------------|----------|
| PI | JP 2004210660 | A | ✓ 20040729 | JP 2002-379498 | 20021227 |
| PRAI | JP 2002-379498 | | 20021227 | | |
| AB | The title compound, Trandolapril benzyl ester, was prepared by reaction of (2s,3aR,7aS)-hexahydro-2-indolinecarbon acid benzyl ester with N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanyl-N-carboxy anhydride as an antihypertensive agent. | | | | |

✓ L36 ANSWER 68 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN - CHECKED DOC
AN 2004:490720 CAPLUS Full-text
DN 141:59698
TI ACE inhibitors having antioxidant and NO-donor activity and use for cardiovascular, renal and diabetes-associated disorders
IN Haj-Yehia, Abdullah Ibrahim; Khan, Mohamed Amin; Qadri, Bashir Ali
PA Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

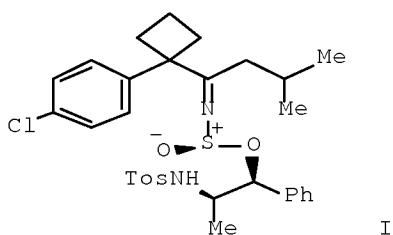
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|-----------------|----------|
| PI | WO 2004050084 | A2 | 20040617 | WO 2003-IL1006 | 20031127 |
| | WO 2004050084 | A3 | 20040930 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003286389 A1 20040623 AU 2003-286389 20031127
EP 1578413 A2 20050928 EP 2003-777134 20031127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 20060166894 A1 20060727 US 2005-536628 20051219
PRAI US 2002-429864P P 20021129
US 2002-430003P P 20021129
WO 2003-IL1006 W 20031127
OS MARPAT 141:59698
AB The present invention provides multifunctional ACE inhibitor compds. that combine ACE-inhibiting activity with capability to scavenge superoxide and other reactive oxygen species, and that may further function as nitric oxide (NO) donors. The compds. are useful for preventing or treating various disorders, including cardiovascular, and diabetes-associated disorders. This invention is further directed to a method for treating and preventing a disorder in which treatment with an ACE inhibitor is indicated, and mainly cardiovascular disorders, renal disorders, and diabetes-associated disorders. The use of said compds. in the preparation of a medicament is further provided.

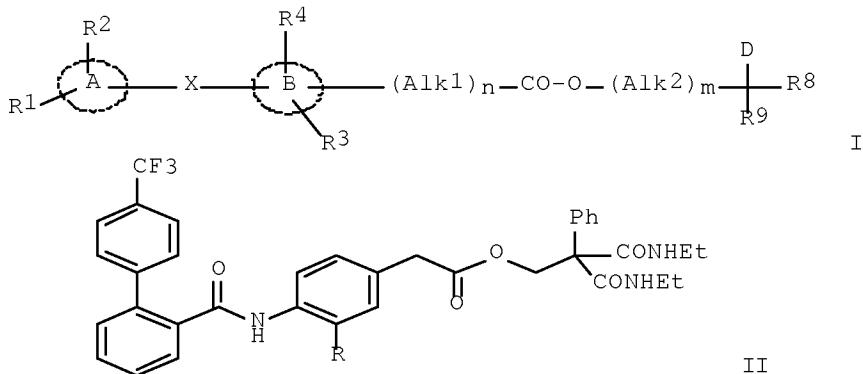
✓ L36 ANSWER 69 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders

✓ L36 ANSWER 70 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of N-phenyl or N-heterocyclyldibenzylamine compounds as inhibitors of cholesteryl ester transfer protein (CETP) and medicinal use thereof

✓ L36 ANSWER 71 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Method of preparing amine stereoisomers via reduction of sulfinylimines in presence of chiral auxiliaries



✓ L36 ANSWER 72 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 TI ✓ Preparation of [4-(1,1'-biphenyl-2-ylcarbonylamino or benzoylamino)phenyl]acetic acid esters as microsomal triglyceride transfer protein (MTP) inhibitors



✓ L36 ANSWER 73 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 TI M✓ Methods of treating or preventing a cardiovascular condition using a cyclooxygenase-1 inhibitor

L36 ANSWER 74 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:255129 CAPLUS [Full-text](#)
 DN 138:271979

TI Method for producing enalapril and related angiotensin converting enzyme inhibitors
 IN Tien, Mong-Jong; Liu, Yu-Liang
 PA Everlight USA, Inc., USA

SO U.S., 7 pp.
CODEN: USXXAM

DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---------------------|------|----------|-----------------|----------|
| PI | US 6541635 | B1 | 20030401 | US 2002-178369 | 20020625 |
| PRAI | TW 2002-91106399 | A | 20020329 | | |
| OS | CASREACT 138:271979 | | | | |

AB The invention discloses a method for producing angiotensin converting enzyme inhibitors (S)-PhCH₂CH₂CH(CO₂Et)-L-Ala-R (NEPA-R) and pharmaceutically-acceptable salts via deprotection of carboxy group-protected derivs. in non-aqueous medium. The product is obtained in high yield with minimal byproduct formation. Thus, NEPA-L-Pro-OSiMe₃, prepared by coupling of NEPA-NCA with H-L-Pro-OSiMe₃, was stirred with isopropanol at room temperature and treated with maleic acid to afford 87.1% enalapril maleate.

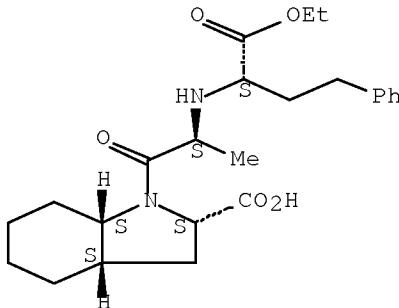
IT 80876-01-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation);
PREP (Preparation)

(preparation of enalapril and related angiotensin converting enzyme inhibitors via deprotection of silyl esters)

RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

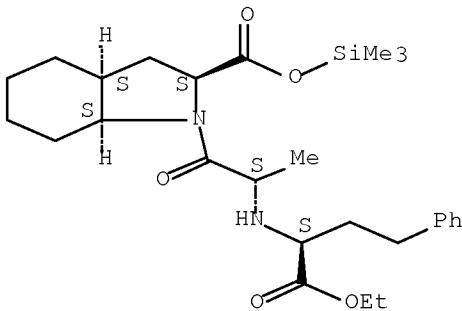


IT 503322-60-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation of enalapril and related angiotensin converting enzyme inhibitors via deprotection of silyl esters)

RN 503322-60-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, trimethylsilyl ester,
(2S,3aS,7aS)- (CA INDEX NAME)

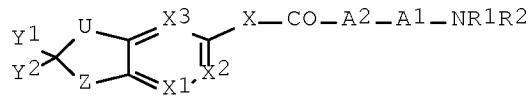
Absolute stereochemistry.



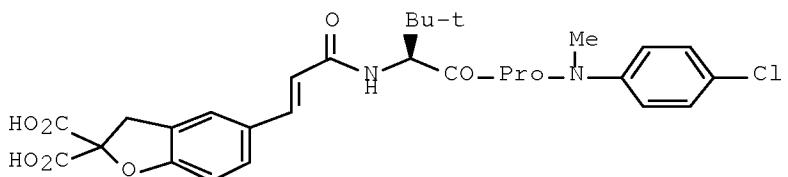
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ L36 ANSWER 75 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Compositions comprising a polypeptide and an active agent

✓ L36 ANSWER 76 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of peptides as STAT modulators



I



II

✓ L36 ANSWER 77 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Compositions comprising a polypeptide and an active agent

✓ L36 ANSWER 78 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of amino acid salts soluble in organic solvents and their
use in dipeptide synthesis

√ L36 ANSWER 79 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Cobalamin compounds useful as cardiovascular agents and as imaging agents

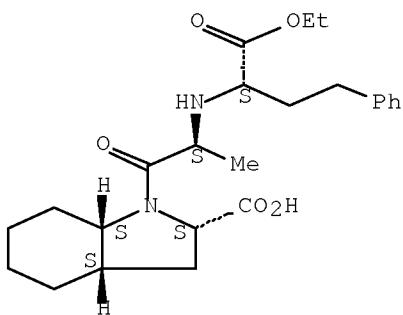
L36 ANSWER 80 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:880052 CAPLUS Full-text
DN 136:279663
TI Procedure for the synthesis of ACE-inhibitors
AU Coll, Alberto Palomo; Morte, Sonia Serra
CS Centro Genesis para la Investigacion, S. L., Barcelona, 08021, Spain
SO Afinidad (2001), 58(495), 391-393
CODEN: AFINAE; ISSN: 0001-9704
PB Asociacion de Quimicos del Instituto Quimico de Sarria
DT Journal
LA Spanish
OS CASREACT 136:279663
AB A new simple and economic synthesis of Enalapril maleate and Trandolapril sulfate in 85% yield is described.
IT 406218-99-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of ACE-inhibitors)
RN 406218-99-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, sulfate (2:1)
(CA INDEX NAME)

CM 1

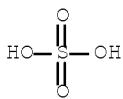
CRN 80876-01-3
CMF C24 H34 N2 O5

Absolute stereochemistry.



CM 2

CRN 7664-93-9
CMF H2 O4 S

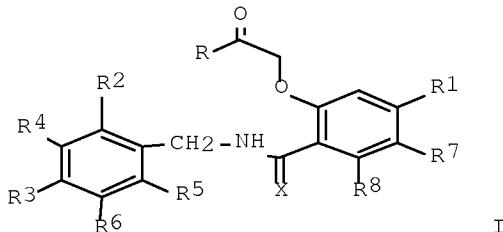


RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

√ L36 ANSWER 81 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ STAT4 and STAT6 binding dipeptide derivatives

√ L36 ANSWER 82 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

√ L36 ANSWER 83 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Preparation and effect of Substituted phenoxyacetic acids in complications arising from diabetes mellitus



√ L36 ANSWER 84 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

√ L36 ANSWER 85 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

✓ L36 ANSWER 86 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI ✓ Combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease

L36 ANSWER 87 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1999:705055 CAPLUS Full-text

DN 131:322920

TI Process for preparing N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine derivatives

IN Yang, Suh-Wan; Chang, Yu-An; Liu, Yu-Liang

PA Everlight USA, Inc., USA

SO U.S., 6 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|-------|-----------------|-------|
| ----- | ---- | ----- | ----- | ----- |

PI US 5977380 A 19991102 US 1999-251341 19990217

PRAI US 1999-251341 19990217

OS CASREACT 131:322920; MARPAT 131:322920

AB (S)-EtO₂CCH(CH₂CH₂Ph)-Ala-R (I; R are certain cyclic amino acids, e.g., L-proline) or their pharmaceutically acceptable salts were prepared by coupling I (R = OC₆H₄R₁, where R₁ is nitro, cyano, sulfite, carboxy, aldehyde, ester, or halo) with an amino acid. Thus, I (R = OC₆H₄NO₂-p), formed by esterifying the acid with 4-nitrophenol in the presence of triethylamine and thionyl chloride in dichloromethane, was treated with L-proline to afford I (R = proline residue) (enalapril).

IT 80876-01-3P

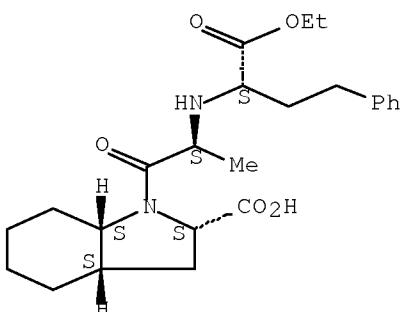
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of [(ethoxycarbonyl)phenylpropyl]-L-alanine derivs.)

RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 88 OF 111 CAPLUS COPYRIGHT 2008 ACS on

STN

AN 1998:38475 CAPLUS Full-text

DN 128:61791

TI Method for the production of L-alanine derivatives with an ACE inhibitor effect

IN Palomo Coll, Alberto; Serra Mortes, Sonia

PA KRKA Tovarna Zdravil D. D., Slovenia

SO Ger. Offen., 6 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|------|----------|------------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| PI DE 19721290 | A1 | 19971211 | DE 1997-19721290 | 19970521 |
| PRAI SI 1996-169 | A | 19960522 | | |

OS MARPAT 128:61791

AB Title compds. R₁CH₂CH₂CH(CO₂Et)NHCH(CH₃)COR₂ [(I): R₁ = alkyl, aryl, heterocycle; R₂ = (un)natural α-amino acid], and their pharmaceutically acceptable salts were prepared as ACE-inhibitors (no data). Thus, (S,S)-I (R₁ = Ph; R₂ = OH) was reacted with L-proline to yield (S,S)-I (R₁ = Ph; R₂ = L-proline), which was converted to its maleate salt.

IT 87679-37-6P 200423-23-0P

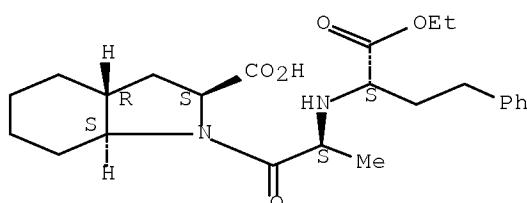
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of L-alanine derivs. with an ACE inhibitor effect)

RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 200423-23-0 CAPLUS

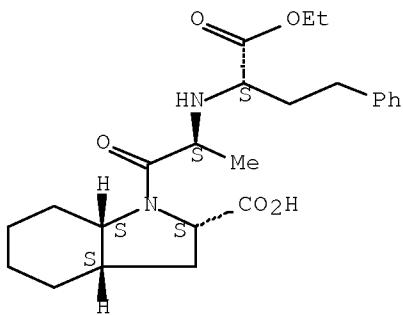
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aβ,7aβ]]-, sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 80876-01-3

CMF C24 H34 N2 O5

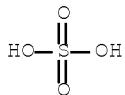
Absolute stereochemistry.



CM 2

CRN 7664-93-9

CMF H2 O4 S



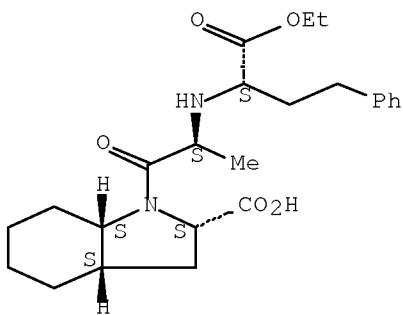
IT 80876-01-3P

RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of L-alanine derivs. with an ACE inhibitor effect)

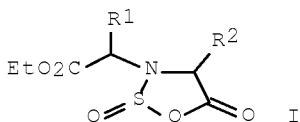
RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



✓ L36 ANSWER 89 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Preparation of carboxylic α -N-sulfino cyclic anhydrides as ACE inhibitor intermediates



L36 ANSWER 90 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1992:651183 CAPLUS [Full-text](#)

DN 117:251183

OREF 117:43483a, 43486a

TI Stereoselective synthesis of a trans-octahydroindole derivative, precursor of Trandolapril (RU 44 570), an inhibitor of angiotensin converting enzyme

AU Brion, F.; Marie, C.; Mackiewicz, P.; Roul, J. M.; Buendia, J.

CS Roussel Uclaf, Romainville, 93230, Fr.

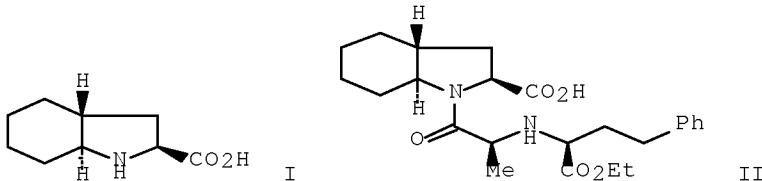
SO Tetrahedron Letters (1992), 33(34), 4889-92
CODEN: TELEAY; ISSN: 0040-4039

DT Journal

LA English

OS CASREACT 117:251183

GI



AB A stereoselective synthesis of the trans-octahydroindole-2-carboxylic acid I a key intermediate in the elaboration of Trandolapril (RU 44 570) (II) was achieved. The optically active starting material used was obtained from meso-di-Me 1,2-cyclohexanedicarboxylate by an enzymic hydrolysis.

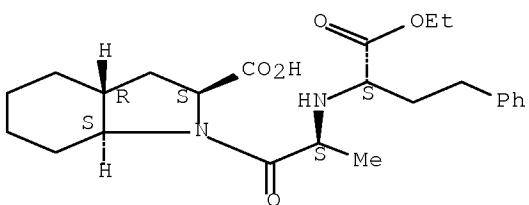
IT 87679-37-6P, Trandolapril

RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective synthesis of)

RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

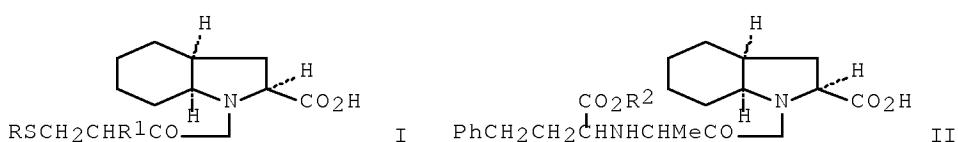


- √ L36 ANSWER 91 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 TI √ Preparation and formulation of [(mercaptoalkyl)carbamoyl]benzoates as analgesics and cardiovascular agents
- √ L36 ANSWER 92 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 TI √ Preparation of disulfide derivatives of mercaptoacylamino acids as cardiovascular agents
- √ L36 ANSWER 93 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 TI √ Preparation of tripeptides with N terminal carbamoyl or acyl groups as renin inhibitors
- √ L36 ANSWER 94 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 TI √ Preparation of carboxyalkyl dipeptides useful as angiotensin-converting enzyme (ACE) inhibitors
- √ 36 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 TI √ Ester prodrug derivatives of carboxylic acid drugs
 AB Ester derivs. $\text{RCO}_2(\text{CH}_2)_n\text{CONR}_1\text{R}_2$ [RCO_2 = acyloxy residue of a carboxylic acid drug; R_1, R_2 = (substituted) alkyl, alkenyl, aryl, aralkyl, or cycloalkyl, or R_1NR_2 = (substituted) ring optionally containing addnl. N, O, or S; $n = 1-3$] are prodrugs of carboxylic acid drugs RCO_2H which are highly stable in aqueous solution but highly susceptible to enzymic hydrolysis in vivo. They are less irritating to the mucosa than the parent drugs and may provide improved bioavailability. The plasma concentration of naproxen in rabbits reached a peak of 7.4 $\mu\text{g}/\text{mL}$ 100 min after oral administration of naproxen (4.8 mg/kg), compared to a peak value of 8.3 $\mu\text{g}/\text{mL}$ 50 min after oral administration of an equivalent amount of naproxen N,N-bis(β -hydroxyethyl)glycolamide ester (I). The half-life for hydrolysis of I in 80% human plasma at 37° and pH 7.4 was 1.3 min. I was prepared by reaction of naproxen and $\text{ClCH}_2\text{CON}(\text{CH}_2\text{CH}_2\text{OH})_2$.

- ✓ L36 ANSWER 96 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- ✓ TI Neutral metalloendopeptidase inhibitors in the treatment of hypertension,
compositions and kits containing the inhibitors, manufacture of the compositions, compounds of the compositions and their preparation
- ✓ AB Neutral metalloendopeptidase (NMEP) inhibitor is used alone or combined with an atrial peptide or an angiotensin converting enzyme (ACE) inhibitor for preparation of pharmaceutical compns. for treating hypertension. The compns. are obtained by mixing a NMEP inhibitor, alone or combined with an atrial peptide or ACE inhibitor, with a pharmaceutically acceptable carrier. S-(4-Methylbenzyl)-L-cysteine, Me ester hydrochloride was prepared by adding thionyl chloride dropwise to N-tert-butyloxycarbonyl-S-(4-methylbenzyl)-L-cysteine in MeOH, heating the mixture under reflux for 90 min, cooling to room temperature, and concentrating in vacuo. Rats with induced hypertension were dosed s.c. with N-(N-[L-1-(2,2-dimethyl-1-oxopropoxy)methoxy]carbonyl)-2-phenylethyl)-L-phenylalanine]- β -alanine and 1-[(2S)-3-mercaptop-2-methyl-1-oxypropyl]-L-proline in Me cellulose vehicle to give a 1-, 2-, 3-, and 4-h decrease in blood pressure of 14, 19, 19, and 15 mMhg vs. an increase of 14, 11, 11, and 8 with the NMEP inhibitor alone and a decrease of 11, 7, 1, and 1 mMhg with the ACE inhibitor alone.

L36 ANSWER 97 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1987:407555 CAPLUS Full-text
 DN 107:7555
 OREF 107:1399a,1402a
 TI Synthesis and structure activity relationships of potent new angiotensin converting enzyme inhibitors containing saturated bicyclic amino acids
 AU Blankley, C. J.; Kaltenbronn, J. S.; DeJohn, D. E.; Werner, A.; Bennett, L. R.; Bobowski, G.; Krolls, U.; Johnson, D. R.; Pearlman, W. M.
 CS Dep. Chem., Warner-Lambert/Parke-Davis Pharm. Res., Ann Arbor, MI, 48105, USA
 SO Journal of Medicinal Chemistry (1987), 30(6), 992-8
 CODEN: JMCMAR; ISSN: 0022-2623
 DT Journal
 LA English
 OS CASREACT 107:7555
 GI



AB The synthesis of a series of angiotensin-converting enzyme (ACE) inhibitors containing saturated bicyclic amino acids in place of proline is described. Octahydroindole-2-carboxylic acid, octahydroisoindole-1-carboxylic acid, and octahydro-3-oxoisoindole-1-carboxylic acid can replace proline in both sulfhydryl and nonsulfhydryl compds.; e.g., sulfhydryl compds. I (R = Ac, H; R1 = H, Me) and nonsulfhydryl compds. II (R2 = Et, H) were prepared. Many of the compds. were equipotent to captopril and enalapril in both in vitro and in vivo ACE-inhibiting activity. Structure-activity relationships are discussed. Indolapril II (R2 = Et) has advanced to clin. evaluation.

IT 80828-34-8P 80876-05-7P 80923-95-1P
108449-50-9P 108449-51-0P 108449-52-1P
108449-53-2P

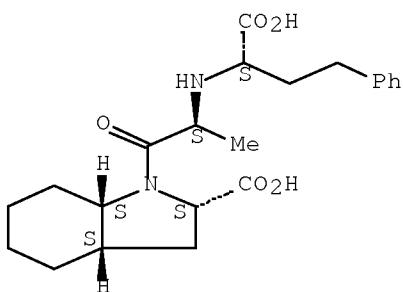
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and angiotensin converting enzyme-inhibiting activity of)

RN 80828-34-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

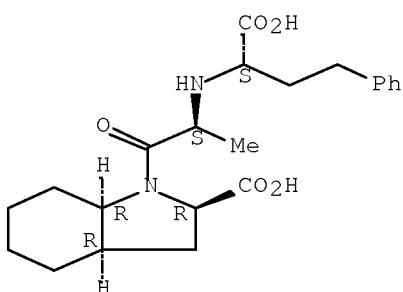
Absolute stereochemistry.



RN 80876-05-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2a,3aβ,7aβ]]- (9CI)
(CA INDEX NAME)

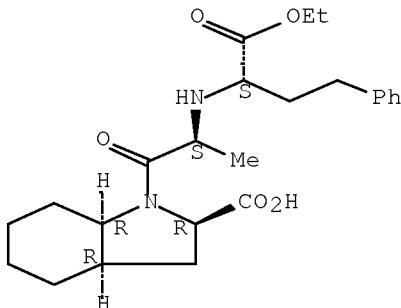
Absolute stereochemistry.



RN 80923-95-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2 α ,3 $\alpha\beta$,7 $\alpha\beta$]]- (9CI) (CA INDEX NAME)

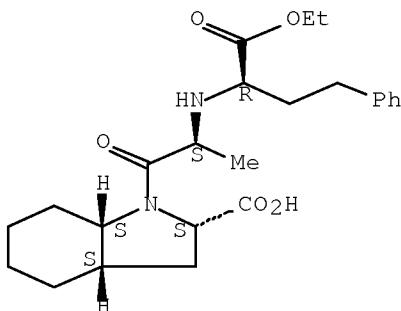
Absolute stereochemistry.



RN 108449-50-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2 α ,3 $\alpha\beta$,7 $\alpha\beta$]]- (9CI) (CA INDEX NAME)

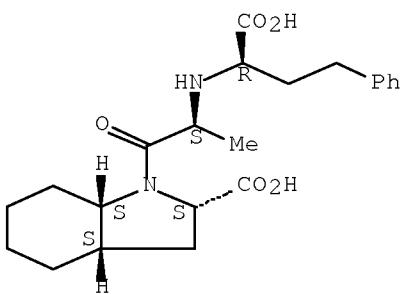
Absolute stereochemistry.



RN 108449-51-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2 α ,3 $\alpha\beta$,7 $\alpha\beta$]]- (9CI) (CA INDEX NAME)

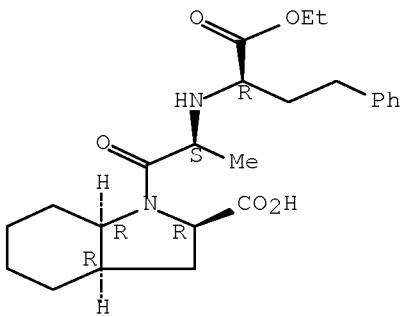
Absolute stereochemistry.



RN 108449-52-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, monohydrochloride,
[2R-[1[S*(R*)], 2α, 3αβ, 7αβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

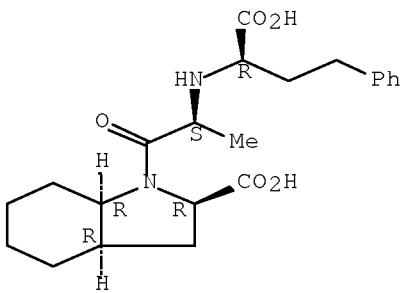


● HCl

RN 108449-53-2 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2R-[1[S*(R*)], 2α, 3αβ, 7αβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

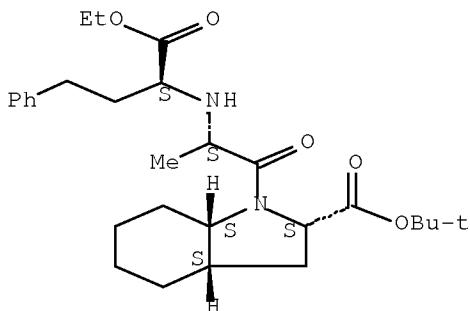


IT 80828-33-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

RN 80828-33-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester,
[2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

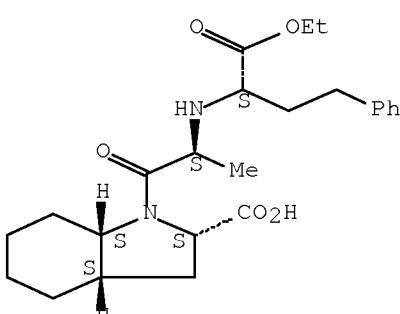


IT 80828-32-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and saponification and angiotensin converting enzyme-inhibiting activity of)

RN 80828-32-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1),
(2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

STNAN 1987:85063 CAPLUS Full-text

DN 106:85063

OREF 106:13977a,13980a

TI A new method of obtaining N-acylated proline derivatives

IN Tremul Lozano, Jesus

PA Lazlo Internacional S. A., Spain

SO Span., 8 pp.

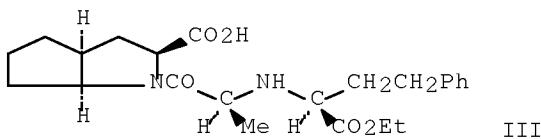
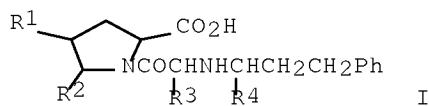
CODEN: SPXXAD

DT Patent

LA Spanish

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------|------|----------|-----------------|----------|
| PI ES 549789 | A1 | 19860316 | ES 1985-549789 | 19851210 |
| PRAI ES 1985-549789 | | 19851210 | | |
| GI | | | | |



AB Title derivs. I [R1, R2 = H, alkyl; R1R2 = (CH₂)_n; n = 3, 4; R3 = alkyl, (CH₂)_mNH₂; m = 3, 4; R4 = OH, alkoxy] are prepared by reacting the corresponding acids (NH₂-protected as needed) with 1-(2-nitrophenylsulfonyloxy)-6-nitrobenzotriazole (II) in the presence of a base, followed by treatment of the resulting intermediates *in situ* with the corresponding CO₂H-protected amino acids and addnl. base, and final deprotection. Thus, a mixture of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-(S)-alanine, II, and Et₃N in MeCN was stirred and treated with a solution of benzyl cis-octahydrocyclopenta[b]pyrrole-2(S)-carboxylate and Et₃N in MeCN, followed by workup involving catalytic hydrogenation, to give peptide derivative III.

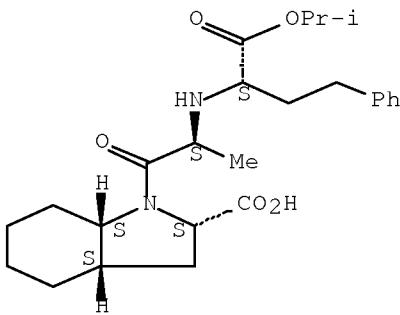
IT 106554-58-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, by peptide coupling with benzotriazolyl sulfonate derivative)

RN 106554-58-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, octahydro-1-[2-[[1-[(1-methylethoxy)carbonyl]-3-phenylpropyl]amino]-1-oxopropyl]-, [2S-[1[R*(R*)]],2α,3αβ,7a.b eta.]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



**L36 ANSWER 99 OF 111 CAPLUS COPYRIGHT 2008 ACS on
STN**

AN 1987:67669 CAPLUS [Full-text](#)

DN 106:67669

OREF 106:11147a,11150a

TI Indolapril

IN Linan Castellet, Isidro; Oliver Mir, Monica

PA Farmhispania S. A., Spain; Bioiberica S. A.

SO Span., 13 pp.

CODEN: SPXXAD

DT Patent

LA Spanish

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------|------|----------|-----------------|----------|
| PI ES 537841 | A1 | 19860116 | ES 1984-537841 | 19841121 |
| PRAI ES 1984-537841 | | 19841121 | | |

AB The title compound, useful as an antihypertensive (no data), was prepared. An indole-2-carboxylic acid derivative was N-acylated by MeCHBrCOBr and NaHCO₃ and the product was treated with (S)-PhCH₂CH₂CH(NH₂)CO₂Et and Et₃N to give Indolapril.

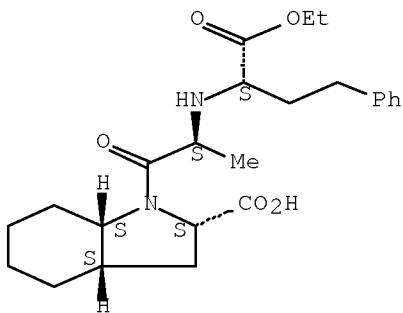
IT 80876-01-3P, Indolapril

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation of, as antihypertensive)

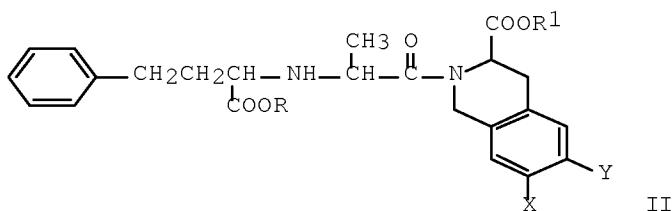
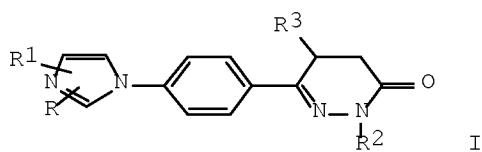
RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



✓ L36 ANSWER 100 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI ✓ Medicaments and method of treating heart failure



✓ L36 ANSWER 101 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
✓ TI Treatment of coronary insufficiency
IN Henning, Rainer; Urbach, Hansjoerg; Teetz, Volker; Geiger, Rolf;
Schoelkens, Bernward

L36 ANSWER 102 OF 111 CAPLUS COPYRIGHT 2008 ACS
on STN

AN 1985:560859 CAPLUS Full-text

DN 103:160859

OREF 103:25849a, 25852a

TI N-Alkylated dipeptides and their esters

IN Teetz, Volker; Wissmann, Hans; Urbach, Hansjoerg

PA Hoechst A.-G. , Fed. Rep. Ger.

SO Eur. Pat. Appl., 33 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

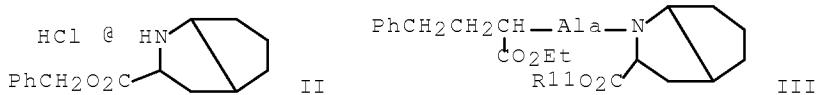
PATENT

KIND DATE

APPLICATION NO.

DATE

| | | | | | |
|------|---|----|----------|-----------------|----------|
| PI | EP 135182 | A2 | 19850327 | EP 1984-110678 | 19840907 |
| | EP 135182 | A3 | 19860305 | | |
| | EP 135182 | B1 | 19880727 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | DE 3333454 | A1 | 19850411 | DE 1983-3333454 | 19830916 |
| | AT 35997 | T | 19880815 | AT 1984-110678 | 19840907 |
| | HU 36145 | A2 | 19850828 | HU 1984-3415 | 19840910 |
| | HU 201565 | B | 19901128 | | |
| | FI 8403590 | A | 19850317 | FI 1984-3590 | 19840913 |
| | FI 80464 | B | 19900228 | | |
| | FI 80464 | C | 19900611 | | |
| | CA 1338163 | C | 19960312 | CA 1984-463078 | 19840913 |
| | DK 8404405 | A | 19850317 | DK 1984-4405 | 19840914 |
| | DK 164939 | B | 19920914 | | |
| | DK 164939 | C | 19930201 | | |
| | NO 8403662 | A | 19850318 | NO 1984-3662 | 19840914 |
| | NO 167743 | B | 19910826 | | |
| | NO 167743 | C | 19911204 | | |
| | AU 8433070 | A | 19850321 | AU 1984-33070 | 19840914 |
| | AU 576782 | B2 | 19880908 | | |
| | JP 60089497 | A | 19850520 | JP 1984-191868 | 19840914 |
| | JP 07098835 | B | 19951025 | | |
| | ZA 8407257 | A | 19850529 | ZA 1984-7257 | 19840914 |
| | ES 535917 | A1 | 19851001 | ES 1984-535917 | 19840914 |
| | IL 72947 | A | 19890228 | IL 1984-72947 | 19840914 |
| | US 5068351 | A | 19911126 | US 1990-560004 | 19900727 |
| PRAI | DE 1983-3333454 | A | 19830916 | | |
| | EP 1984-110678 | A | 19840907 | | |
| | US 1984-650715 | B1 | 19840914 | | |
| | US 1986-943882 | B1 | 19861219 | | |
| | US 1988-178767 | B1 | 19880330 | | |
| | US 1989-403919 | B1 | 19890907 | | |
| OS | MARPAT 103:160859 | | | | |
| GI | | | | | |



AB Title compds. R₃O₂CCHR₄NR₅COCHR₁NHCH(CO₂R₂)(CH₂)_nR [n = 1, 2; R = H, (un)substituted C₁-8 aliphatic, C₃-9 alicyclic, C₆-12 aromatic, C₇-14 araliph., or C₇-14 alicyclic aliphatic residue, OR₆, SR₆ [R₆ = (un)substituted C₁-4 aliphatic, C₆-12 aromatic, or heteroarom. residue]; R₁ = H, (un)substituted C₁-6 aliphatic, C₃-9 alicyclic, C₄-13 alicyclic aliphatic, C₆-12 aromatic, C₇-16 araliph., or heteroarom. residue, amino acid side chain; R₂, R₃ = H, (un)substituted C₁-6 aliphatic, C₃-9 alicyclic, C₆-12 aromatic, or C₇-16 araliph. residue; CHR₄NR₅ = C₅-15 heterocyclic mono-, bi-, or tricyclic ring system] were prepared via the condensation of HO₂CCHR₁NHCH(CO₂R₂)(CH₂)_nR with R₃O₂CCHR₄NHR₅ in the presence of phosphinic acid anhydrides R₇R₈P(O)OP(O)R₉R₁₀ (R₇, R₈, R₉, R₁₀ = alkyl or aralkyl). Thus, (S,S,S)-azabicyclo[3.3.0]octane II was condensed with (S)-PhCH₂CH₂CH(CO₂Et)-(S)-Ala-OH by ethylmethylphosphinic acid anhydride in CH₂C₁₂ containing Et₃N to give peptide III (R₁₁ = CH₂Rh), which was debenzylated to give III (R₁ = H). I

inhibit angiotensin-converting enzyme and can be used as antihypertensives (no data).

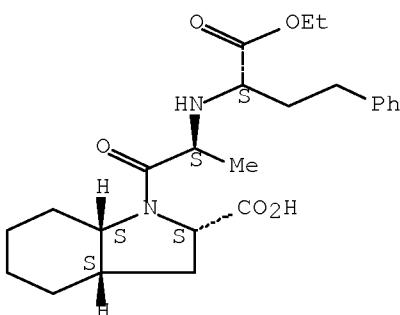
IT 80828-32-6P 83542-05-6P 98677-37-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 80828-32-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1),
(2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

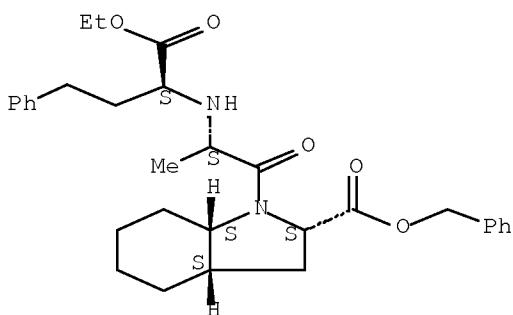


● HCl

RN 83542-05-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
[2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

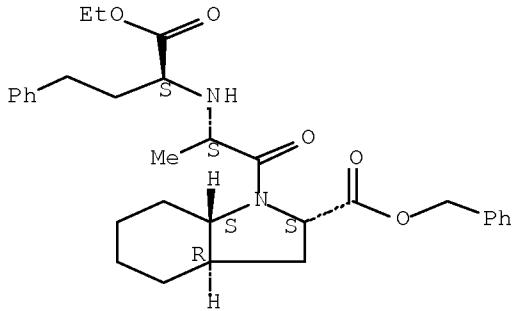
Absolute stereochemistry.



RN 98677-37-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
(2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



**L36 ANSWER 103 OF 111 CAPLUS COPYRIGHT 2008 ACS
on STN**

AN 1985:560858 CAPLUS Full-text

DN 103:160858

OREF 103:25849a,25852a

TI N-Alkylated dipeptides and their esters

IN Urbach, Hansjoerg; Henning, Rainer; Wissmann, Hans; Teetz, Volker

PA Hoechst A.-G., Fed. Rep. Ger.

SO Eur. Pat. Appl., 32 pp.

CODEN: EPXXDW

DT Patent

LA German

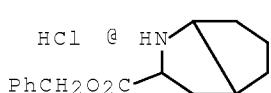
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | EP 135181 | A2 | 19850327 | EP 1984-110677 | 19840907 |
| | EP 135181 | A3 | 19860402 | | |
| | EP 135181 | B1 | 19900131 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | DE 3333455 | A1 | 19850411 | DE 1983-3333455 | 19830916 |
| | AT 49979 | T | 19900215 | AT 1984-110677 | 19840907 |
| | HU 36140 | A2 | 19850828 | HU 1984-3417 | 19840910 |
| | HU 198303 | B | 19890928 | | |
| | FI 8403591 | A | 19850317 | FI 1984-3591 | 19840913 |
| | FI 80275 | B | 19900131 | | |
| | FI 80275 | C | 19900510 | | |
| | CA 1338162 | C | 19960312 | CA 1984-463071 | 19840913 |
| | DK 8404404 | A | 19850317 | DK 1984-4404 | 19840914 |
| | DK 166027 | B | 19930301 | | |
| | DK 166027 | C | 19930712 | | |
| | NO 8403663 | A | 19850318 | NO 1984-3663 | 19840914 |
| | NO 167808 | B | 19910902 | | |
| | NO 167808 | C | 19911218 | | |
| | AU 8433071 | A | 19850321 | AU 1984-33071 | 19840914 |
| | AU 575585 | B2 | 19880804 | | |
| | JP 60089498 | A | 19850520 | JP 1984-191869 | 19840914 |
| | JP 07098836 | B | 19951025 | | |
| | ZA 8407259 | A | 19850529 | ZA 1984-7259 | 19840914 |
| | ES 535918 | A1 | 19851001 | ES 1984-535918 | 19840914 |
| | IL 72946 | A | 19900429 | IL 1984-72946 | 19840914 |
| | US 5055591 | A | 19911008 | US 1988-173024 | 19880323 |
| PRAI | DE 1983-3333455 | A | 19830916 | | |
| | EP 1984-110677 | A | 19840907 | | |

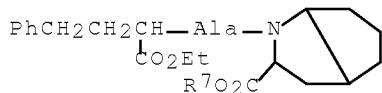
US 1984-650714
US 1986-943881

B1 19840914
B1 19861219

GI



II



III

AB Title compds. R₃O₂CCHR₄NR₅COCHR₁NHCH(CO₂R₂)(CH₂)_nR [I; n = 1, 2; R = H, (un)substituted C₁-8 aliphatic, C₃-9 alicyclic, C₆-12 aromatic, C₇-14 araliph., or C₇-14 alicyclic aliphatic residue, OR₆, SR₆ [R₆ = (un)substituted C₁-4 aliphatic, C₆-12 aromatic, or heteroarom. residue]; R₁ = H, (un)substituted C₃-9 alicyclic, C₄-13 alicyclic aliphatic, C₆-12 aromatic, C₇-16 araliph., or heteroarom. residue, amino acid side chain; R₂, R₃ = H, (un)substituted C₁-6 aliphatic, C₃-9 alicyclic, C₆-12 aromatic, or C₇-16 araliph. residue; CHR₄NR₅ = C₅-15 heterocyclic mono-, bi-, or tricyclic ring system] were prepared via the condensation of HO₂CCHR₁NHCH(CO₂R₂)(CH₂)_nR with R₃O₂CCHR₄NHR₅ in the presence of an alkanephosphoric acid anhydride. Thus, (S,S,S)-azabicyclo[3.3.0]octane II was condensed with (S)-PhCH₂CH₂CH(CO₂Et)-(S)-Ala-OH by n-propanephosphonic acid anhydride in CH₂Cl₂ in the presence of N-ethylmorpholine to give peptide derivative III (R₇ = CH₂Ph), which was debenzylated to give III (R₇ = H) (all-S isomer). I inhibit angiotensin-converting enzyme and can be used as antihypertensives (no data).

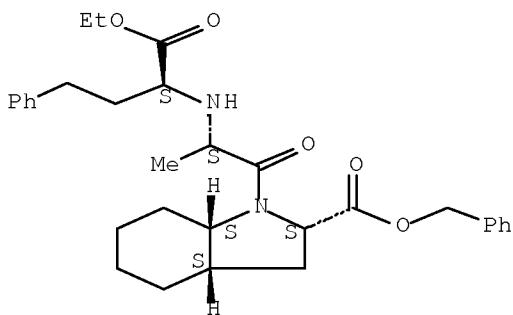
IT 83542-05-6P 98677-37-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 83542-05-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
[2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

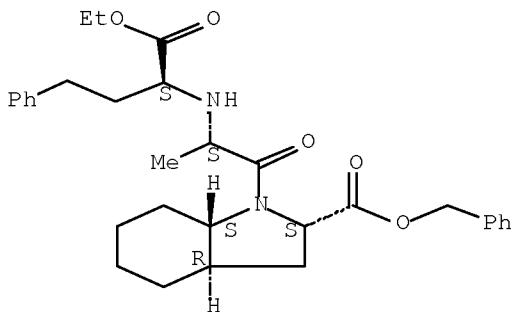
Absolute stereochemistry.



RN 98677-37-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
(2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



**L36 ANSWER 104 OF 111 CAPLUS COPYRIGHT 2008 ACS
on STN**

AN 1985:185278 CAPLUS [Full-text](#)

DN 102:185278

OREF 102:29073a, 29076a

TI Phosphate salts of 1-(2-[(1-alkoxycarbonyl-3-aralkyl)amino]-1-oxoalkyl)octahydro-1H-indole-2-carboxylic acids

IN Seamans, Ronald E.; Behnke, Walter E.

PA Warner-Lambert Co., USA

SO U.S., 5 pp.

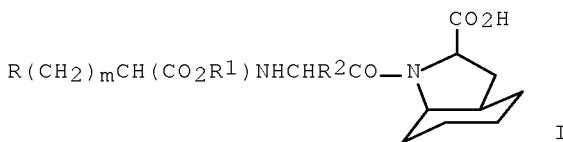
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI US 4490386 | A | 19841225 | US 1982-422499 | 19820923 |
| PRAI US 1982-422499 | | 19820923 | | |
| OS CASREACT 102:185278; MARPAT 102:185278 | | | | |
| GI | | | | |

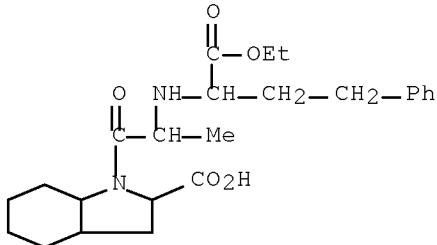


AB One example of a phosphate salt of acylated octahydroindolecarboxylic acids I [R = (un)substituted Ph; m = 0-3; R1 = H, alkyl; R2 = H, alkyl, PhCH2], antihypertensives (no data) was prepared. Thus, the S,S-isomer of Et α-[(1-carboxyethyl)amino]benzenebutanoate hydrochloride was treated with tert-Bu (1-octahydro-1H-indole-2-carboxylate in the presence of 1-hydroxytriazole, Et3N, and dicyclohexylcarbodiimide to give the S,S,S-isomer of I (R = Ph, m = 2, R1 = Et, R2 = Me) as the HCl salt (II). Treating II with 85% H3PO4 gave the 1:1 phosphate salt.

IT 96022-35-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and formation of phosphate salt from)
RN 96022-35-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride (9CI) (CA INDEX NAME)

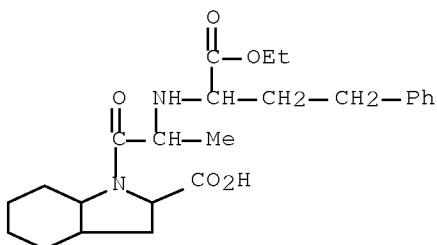


● HCl

IT 96015-97-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 96015-97-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phosphate (1:1) (CA INDEX NAME)

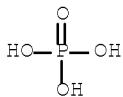
CM 1

CRN 80876-02-4
CMF C24 H34 N2 O5



CM 2

CRN 7664-38-2
CMF H3 O4 P



L36 ANSWER 105 OF 111 CAPLUS COPYRIGHT 2008 ACS
on STN

AN 1984:139616 CAPLUS Full-text

DN 100:139616

OREF 100:21335a, 21338a

TI Derivatives of bicyclic amino acids, agents containing them and their use, as well as bicyclic amino acids as intermediates

IN Urbach, Hansjoerg; Henning, Rainer; Teetz, Volker; Geiger, Rolf; Becker, Reinhard; Gaul, Holger

PA Hoechst A.-G., Fed. Rep. Ger.

SO Eur. Pat. Appl., 103 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | EP 84164 | A2 | 19830727 | EP 1982-112007 | 19821224 |
| | EP 84164 | A3 | 19831012 | | |
| | EP 84164 | B1 | 19870128 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | DE 3151690 | A1 | 19830707 | DE 1981-3151690 | 19811229 |
| | DE 3210701 | A1 | 19831006 | DE 1982-3210701 | 19820324 |
| | EP 170775 | A1 | 19860212 | EP 1985-103730 | 19821224 |
| | EP 170775 | B1 | 19891108 | | |
| | EP 170775 | B2 | 19941012 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | AT 25244 | T | 19870215 | AT 1982-112007 | 19821224 |
| PRAI | DE 1981-3151690 | A | 19811229 | | |
| | DE 1982-3210701 | A | 19820324 | | |
| | EP 1982-112007 | P | 19821224 | | |

OS CASREACT 100:139616

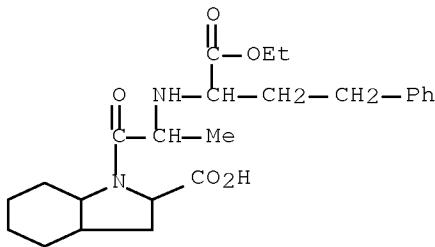
GI For diagram(s), see printed CA Issue.

AB Title compds. I [R = H, C1-6 alkyl, aminoalkyl, C2-6 alkenyl, C5-9 cycloalkyl, C5-9 cycloalkenyl, C5-7 cycloalkyl-C1-4 alkyl, (un)substituted aryl or partially hydrogenated aryl; R1 = H, C1-6 alkyl, C2-6 alkenyl, aryl-C1-4 alkyl; R2 = H, OH; R3 = H; R2R3 = O; R4 = C1-6 alkyl, C2-6 alkenyl, C5-9 cycloalkyl, (un)substituted aryl, indol-3-yl; n = 0, 1, 2] were prepared as antihypertensives due to their ability to inhibit angiotensin-converting enzyme (ACE). Thus, (S)-PhCH₂CH₂CH(CO₂Et)-(S)-Ala-OH was condensed with (d,l)-2β,3αβ,7αβ-octahydroindole-3-carboxylic acid benzyl ester-HCl by DCC/1-hydroxybenzotriazole in DMF containing N-ethylmorpholine to give a mixture of the (2S,3aR,7aR)- and (2R,3aS,7aS)-diastereoisomers of octahydroindole II (R₅ = Et, R₆ = CH₂Ph) (III). (2S,3aR,7aR)-III was debenzylated by hydrogenolysis and then saponified to give (2S,3aR,7aR)-II (R₅ = R₆ = H). (2S,3aR,7aS)-II (R₅ = R₆ = H) inhibited ACE in rats with an ED₅₀ of 800 µg/kg.

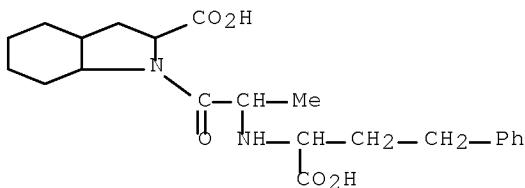
IT 80876-02-4 83601-86-9

RL: RCT (Reactant); RACT (Reactant or reagent)
 (angiotensin converting enzyme-inhibiting activity of)

RN 80876-02-4 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)

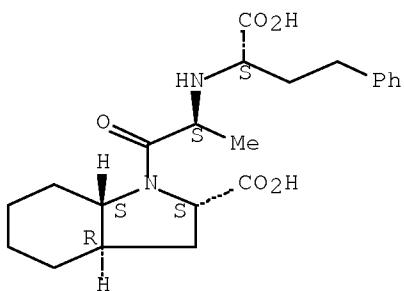


RN 83601-86-9 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



IT 87679-71-8P 87679-72-9P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and angiotensin converting enzyme-inhibiting activity of)
 RN 87679-71-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

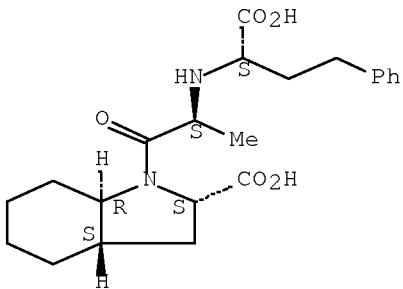
Absolute stereochemistry.



RN 87679-72-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2 α ,3 $\alpha\beta$,7 $\alpha\alpha$]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



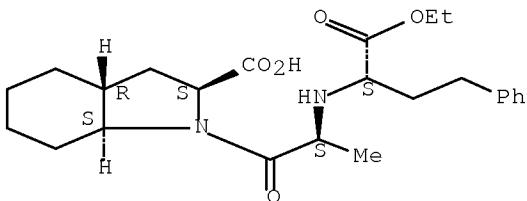
IT 87679-37-6P 87679-42-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and angiotensin-converting enzyme-inhibiting activity of)

RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

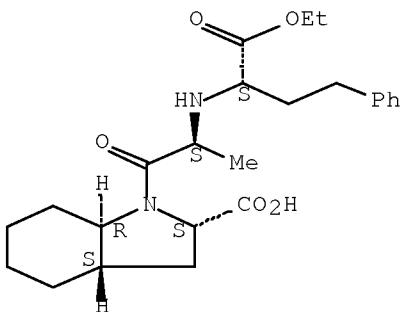
Absolute stereochemistry. Rotation (-).



RN 87679-42-3 CAPLUS

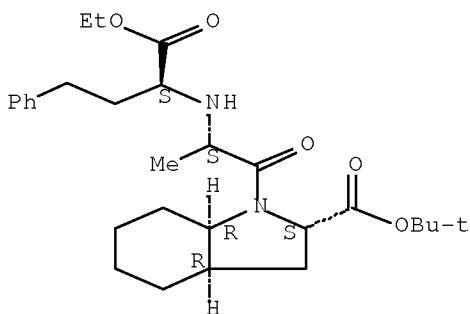
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2 α ,3 $\alpha\beta$,7 $\alpha\alpha$]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



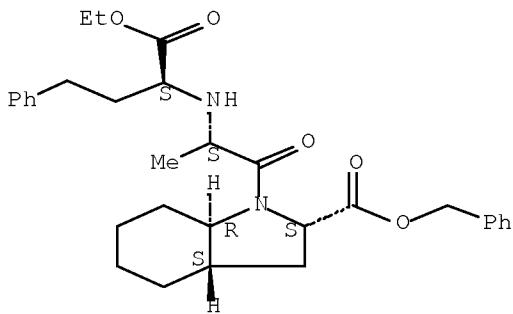
IT 87679-29-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and de-tert-butylation of)
 RN 87679-29-6 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-
 phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester,
 [2S-[1[R*(R*)]],2a,3aa,7aa]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



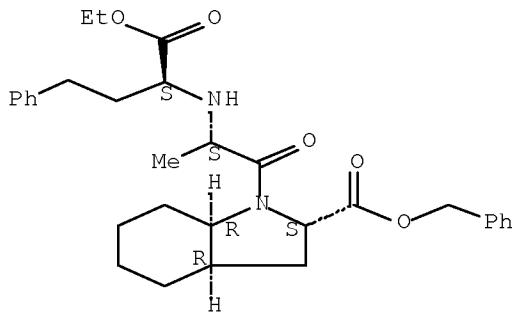
IT 87679-41-2P 87827-53-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and hydrogenolysis of)
 RN 87679-41-2 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-
 phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
 (2S,3aS,7aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 87827-53-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-
 phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
 [2S-[1[R*(R*)]],2a,3aa,7aa]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



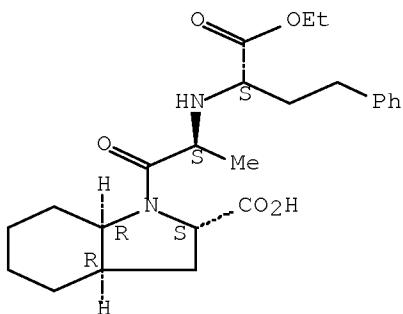
IT 87725-71-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

RN 87725-71-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride,
[2S-[1[R*(R*)],2α,3aa,7aa]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

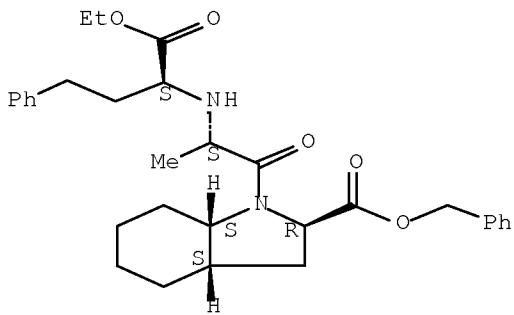
IT 87679-28-5P 87679-32-1P 87679-40-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 87679-28-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
[2R-[1[S*(S*)],2α,3aa,7aa]]- (9CI) (CA INDEX NAME)

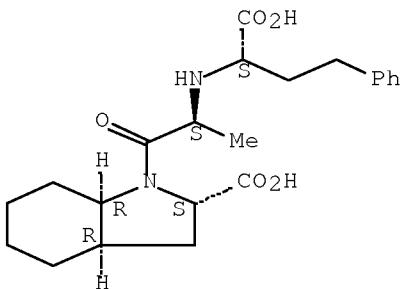
Absolute stereochemistry.



RN 87679-32-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)], 2a, 3aa, 7aa]]- (9CI)
(CA INDEX NAME)

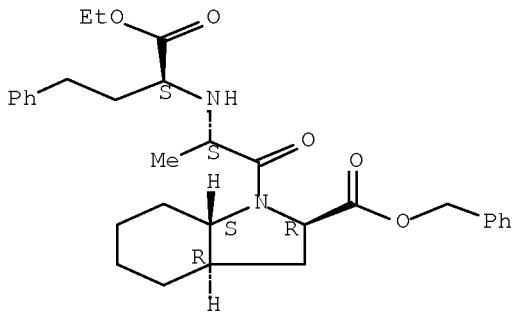
Absolute stereochemistry.



RN 87679-40-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
(2R,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



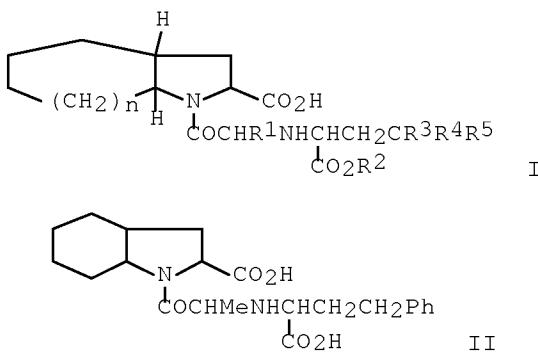
L36 ANSWER 106 OF 111 CAPLUS COPYRIGHT 2008 ACS

on STN

AN 1984:34404 CAPLUS Full-text
 DN 100:34404
 OREF 100:5335a,5338a
 TI Derivatives of bicyclic amino acids, an agent containing them, their use,
 and bicyclic amino acids as intermediates
 IN Urbach, Hansjoerg; Henning, Rainer; Teetz, Volker; Geiger, Rolf; Becker,
 Reinhard
 PA Hoechst A.-G. , Fed. Rep. Ger.
 SO Ger. Offen., 79 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | DE 3151690 | A1 | 19830707 | DE 1981-3151690 | 19811229 |
| | CA 1341296 | C | 20010925 | CA 1982-418453 | 19821223 |
| | AU 8291931 | A | 19830707 | AU 1982-91931 | 19821224 |
| | AU 559140 | B2 | 19870226 | | |
| | EP 84164 | A2 | 19830727 | EP 1982-112007 | 19821224 |
| | EP 84164 | A3 | 19831012 | | |
| | EP 84164 | B1 | 19870128 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | EP 170775 | A1 | 19860212 | EP 1985-103730 | 19821224 |
| | EP 170775 | B1 | 19891108 | | |
| | EP 170775 | B2 | 19941012 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | AT 25244 | T | 19870215 | AT 1982-112007 | 19821224 |
| | AT 47838 | T | 19891115 | AT 1985-103730 | 19821224 |
| | FI 8204474 | A | 19830630 | FI 1982-4474 | 19821227 |
| | FI 80017 | B | 19891229 | | |
| | FI 80017 | C | 19900410 | | |
| | JP 58118569 | A | 19830714 | JP 1982-227179 | 19821227 |
| | JP 05087504 | B | 19931216 | | |
| | ES 518574 | A1 | 19831001 | ES 1982-518574 | 19821227 |
| | IL 67572 | A | 19920818 | IL 1982-67572 | 19821227 |
| | DK 8205767 | A | 19830630 | DK 1982-5767 | 19821228 |
| | DK 170444 | B1 | 19950904 | | |
| | NO 8204394 | A | 19830630 | NO 1982-4394 | 19821228 |
| | NO 156786 | B | 19870817 | | |
| | NO 156786 | C | 19871125 | | |
| | ZA 8209523 | A | 19831026 | ZA 1982-9523 | 19821228 |
| | HU 27438 | A2 | 19831028 | HU 1982-4177 | 19821228 |
| | HU 194278 | B | 19880128 | | |
| | HU 194167 | B | 19880128 | HU 1984-4653 | 19821228 |
| | ES 521740 | A1 | 19840116 | ES 1983-521740 | 19830422 |
| | NO 8302741 | A | 19830630 | NO 1983-2741 | 19830727 |
| | NO 158799 | B | 19880725 | | |
| | NO 158799 | C | 19881102 | | |
| | CA 1206478 | A2 | 19860624 | CA 1984-461836 | 19840824 |
| | US 5008400 | A | 19910416 | US 1984-673605 | 19841121 |
| | FI 8803456 | A | 19880721 | FI 1988-3456 | 19880721 |
| | FI 80675 | B | 19900330 | | |
| | FI 80675 | C | 19900710 | | |
| | JP 01301695 | A | 19891205 | JP 1989-7870 | 19890118 |
| | JP 01301659 | A | 19891205 | JP 1989-7871 | 19890118 |
| | JP 06004586 | B | 19940119 | | |

| | | | | |
|----------------------|----|----------|----------------|----------|
| US 4933361 | A | 19900612 | US 1989-346339 | 19890428 |
| US 5101039 | A | 19920331 | US 1990-468567 | 19900123 |
| DK 9201199 | A | 19920928 | DK 1992-1199 | 19920928 |
| DK 171232 | B1 | 19960805 | | |
| PRAI DE 1981-3151690 | A | 19811229 | | |
| DE 1982-3210701 | A | 19820324 | | |
| CA 1982-418453 | A3 | 19821223 | | |
| EP 1982-112007 | P | 19821224 | | |
| EP 1985-103730 | A | 19821224 | | |
| FI 1982-4474 | A | 19821227 | | |
| US 1982-453092 | B3 | 19821227 | | |
| US 1984-673605 | A1 | 19841121 | | |
| OS MARPAT 100:34404 | | | | |
| GI | | | | |



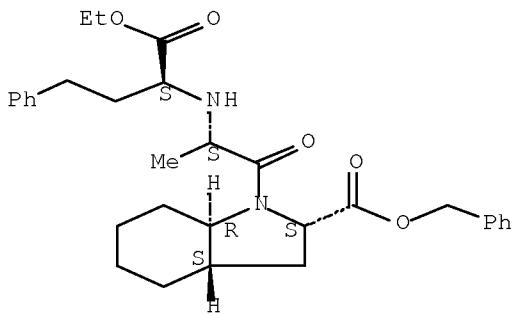
AB Pyrrolecarboxylic acids I [n = 0-2; R1 = H, alkyl (un)substituted by amino, cycloalkyl, or aryl, (un)substituted alkenyl, cycloalk(en)yl, or (partly hydrogenated)aryl, cyclo- or bicyclic heterocyclyl, side-chain of a naturally occurring amino acid; R2 = H, alk(en)yl, arylalkyl; R3 = alk(en)yl, cycloalkyl, (un)substituted aryl; R4 = H, OH; R5 = H, R4R5 = O] and their physiol. tolerable salts, useful as antihypertensives (ED50 40-1080 µg/kg in rats), were prepared N-[1-(S)-Carboxy-3-phenylpropyl]- (S)-alanyl-(2S,3aR,7aR)octahydroindole-2-carboxylic acid II was prepared in 9 steps from indole.

IT 87679-41-2P 87827-53-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and debenzylation of)

RN 87679-41-2 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aR)- (CA INDEX NAME)

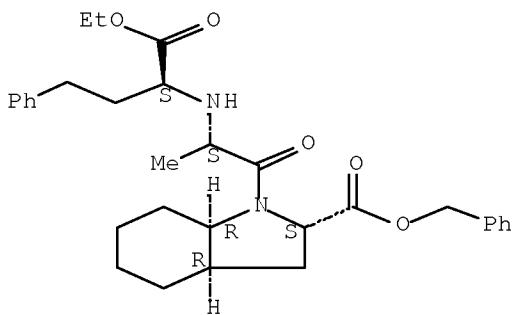
Absolute stereochemistry.



RN 87827-53-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
[2S-[1[R*(R*)], 2α, 3αα, 7αα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



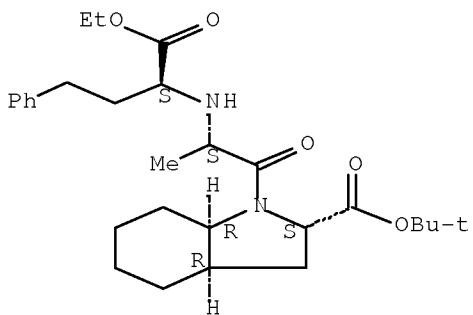
IT 87679-29-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

RN 87679-29-6 CAPLUS

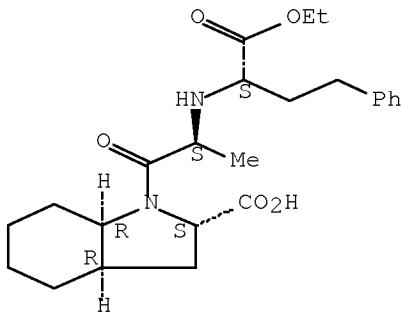
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester,
[2S-[1[R*(R*)], 2α, 3αα, 7αα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 87725-71-1P 87725-72-2P 87725-73-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and saponification of)
 RN 87725-71-1 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-
 phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride,
 [2S-[1[R*(R*)],2 α ,3 α ,7 α]]- (9CI) (CA INDEX NAME)

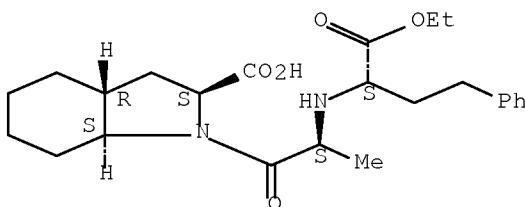
Absolute stereochemistry.



● HCl

RN 87725-72-2 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)-3-
 phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride,
 (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

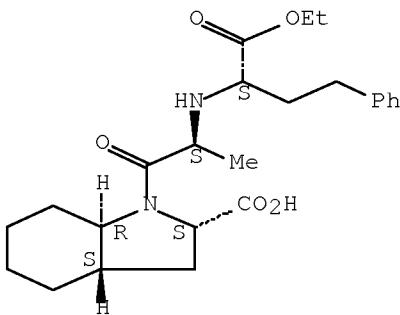
Absolute stereochemistry. Rotation (-).



● HCl

RN 87725-73-3 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-
 phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride,
 [2S-[1[R*(R*)],2 α ,3 β ,7 α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

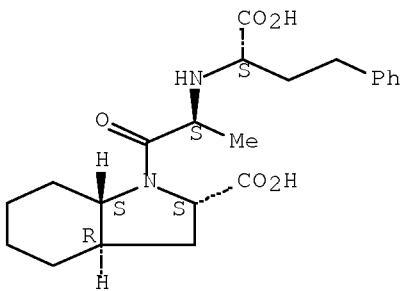
IT 87679-71-8 87679-72-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as antihypertensive)

RN 87679-71-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

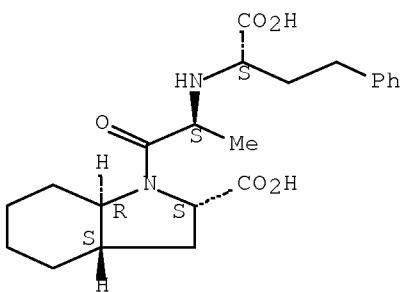
Absolute stereochemistry.



RN 87679-72-9 CAPLUS

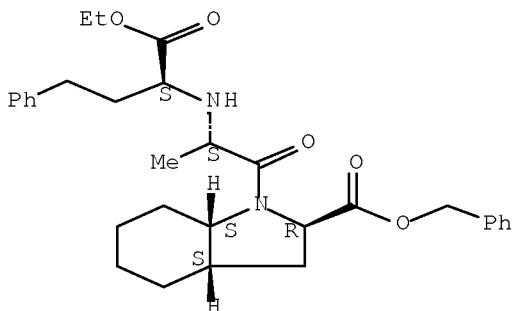
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)], 2α, 3aβ, 7aα]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



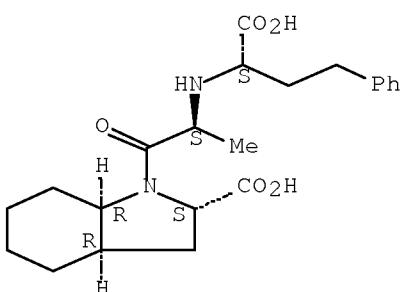
IT 87679-28-5P 87679-32-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 87679-28-5 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
 [2R-[1S*(S*)],2 α ,3 α ,7 α]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 87679-32-1 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

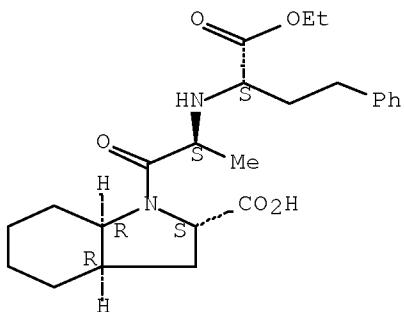
Absolute stereochemistry.



IT 87679-36-5P 87679-37-6P 87679-40-1P
 87679-42-3P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of, as antihypertensive)
 RN 87679-36-5 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-

[1[R*(R*)],2a,3aa,7aa]- (9CI) (CA INDEX NAME)

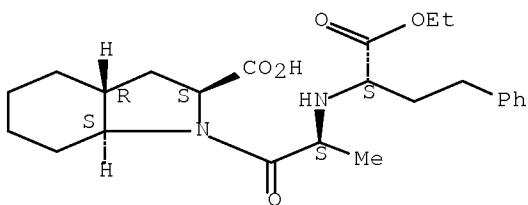
Absolute stereochemistry.



RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

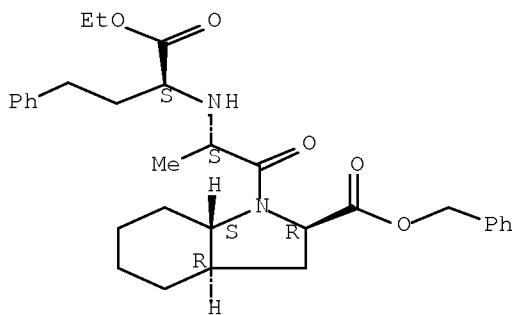
Absolute stereochemistry. Rotation (-).



RN 87679-40-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2R,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

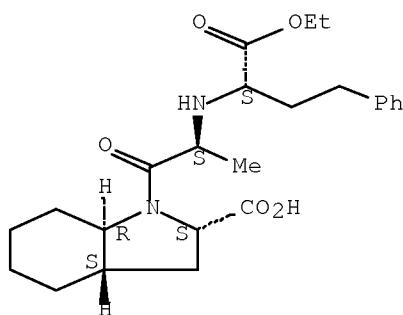


RN 87679-42-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-

phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2 α ,3 $\alpha\beta$,7 $\alpha\alpha$]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



**L36 ANSWER 107 OF 111 CAPLUS COPYRIGHT 2008 ACS
on STN**

AN 1983:143272 CAPLUS Full-text

DN 98:143272

OREF 98:21821a, 21824a

TI Substituted acyl derivatives of octahydro-1H-indole-2-carboxylic acids

IN Hoefle, Milton L.; Bobowski, George

PA Warner-Lambert Co., USA

SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 194,307, abandoned.

CODEN: USXXAM

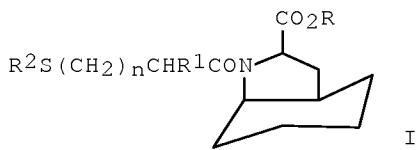
DT Patent

LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | US 4350704 | A | 19820921 | US 1981-233940 | 19810217 |
| | IL 62294 | A | 19860731 | IL 1981-62294 | 19810304 |
| | IL 71045 | A | 19860731 | IL 1981-71045 | 19810304 |
| | ZA 8101493 | A | 19820331 | ZA 1981-1493 | 19810305 |
| | CA 1205476 | A1 | 19860603 | CA 1981-372381 | 19810305 |
| | EP 37231 | A2 | 19811007 | EP 1981-301243 | 19810324 |
| | EP 37231 | A3 | 19820428 | | |
| | EP 37231 | B1 | 19870128 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| | EP 88341 | A1 | 19830914 | EP 1983-101990 | 19810324 |
| | EP 88341 | B1 | 19870722 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | EP 88342 | A1 | 19830914 | EP 1983-101991 | 19810324 |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | AT 25243 | T | 19870215 | AT 1981-301243 | 19810324 |
| | AT 28452 | T | 19870815 | AT 1983-101990 | 19810324 |
| | FI 8100971 | A | 19811003 | FI 1981-971 | 19810330 |
| | FI 76072 | B | 19880531 | | |
| | FI 76072 | C | 19880909 | | |
| | AU 8168939 | A | 19811008 | AU 1981-68939 | 19810331 |
| | AU 543861 | B2 | 19850509 | | |
| | DK 8101482 | A | 19811003 | DK 1981-1482 | 19810401 |
| | DK 157851 | B | 19900226 | | |

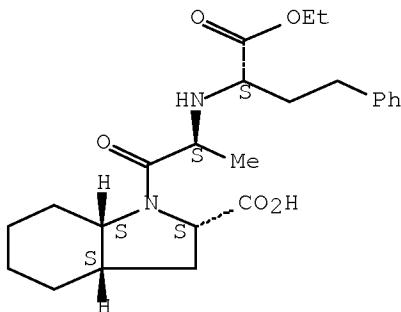
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|------|--------------------|----|----------|----|--------------|
| DK | 157851 | C | 19900730 | | |
| NO | 8101121 | A | 19811005 | NO | 1981-1121 |
| NO | 156609 | B | 19870713 | | 19810401 |
| NO | 156609 | C | 19871021 | | |
| ES | 500965 | A1 | 19820816 | ES | 1981-500965 |
| HU | 25950 | A2 | 19830829 | HU | 1981-846 |
| HU | 183383 | B | 19840428 | | 19810401 |
| HU | 30000 | A2 | 19840228 | HU | 1983-1049 |
| HU | 187880 | B | 19860228 | | 19810401 |
| JP | 56161372 | A | 19811211 | JP | 1981-48512 |
| JP | 02047480 | B | 19901019 | | 19810402 |
| US | 4425355 | A | 19840110 | US | 1981-277794 |
| ES | 504189 | A1 | 19820616 | ES | 1981-504189 |
| DD | 201782 | A5 | 19830810 | DD | 1981-233893 |
| DD | 202146 | A5 | 19830831 | DD | 1981-233892 |
| SU | 1246893 | A3 | 19860723 | SU | 1981-3339202 |
| SU | 1241988 | A3 | 19860630 | SU | 1982-3498497 |
| FI | 8504743 | A | 19851129 | FI | 1985-4743 |
| FI | 76560 | B | 19880729 | | 19851129 |
| FI | 76560 | C | 19881110 | | |
| NO | 8600366 | A | 19811005 | NO | 1986-366 |
| NO | 156898 | B | 19870907 | | 19860203 |
| NO | 156898 | C | 19871216 | | |
| DK | 8800910 | A | 19880222 | DK | 1988-910 |
| DK | 159419 | B | 19901015 | | 19880222 |
| DK | 159419 | C | 19910318 | | |
| PRAI | US 1980-137106 | A2 | 19800402 | | |
| | US 1980-194307 | A2 | 19801006 | | |
| | US 1981-233940 | A | 19810217 | | |
| | EP 1981-301243 | P | 19810324 | | |
| | EP 1983-101990 | A | 19810324 | | |
| | FI 1981-971 | A | 19810330 | | |
| | IL 1984-62294 | A | 19840531 | | |
| OS | CASREACT 98:143272 | | | | |
| GI | | | | | |



- AB The antihypertensive title compds. I [R = H, alkyl; R1 = H, alkyl, PhCH2; R2 = H, R3CO (R3 = alkyl, (un)substituted phenyl); and their pharmaceutically acceptable salts; n = 0, 1] were prepared. Thus, (\pm)-Et (2 α ,3 α β ,7 α β)-octahydro-1H-indole-2-carboxylate, prepared by hydrogenation of Et indole-2-carboxylate, was treated with AcSCH2CH2COCl to give Et (2 α ,3 α β ,7 α β)-octahydro-1-[3-(acetylthio)propanoyl]-1H-indole-2-carboxylate (II). The angiotensin converting enzyme inhibitory IC50 of II was 3.8 + 106 M.
- IT 80828-32-6P 80828-34-8P 80876-03-5P
80876-05-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and angiotensin converting enzyme inhibition by)
- RN 80828-32-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

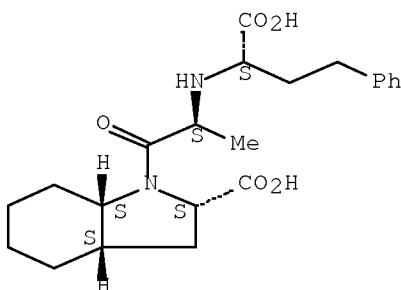


● HCl

RN 80828-34-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

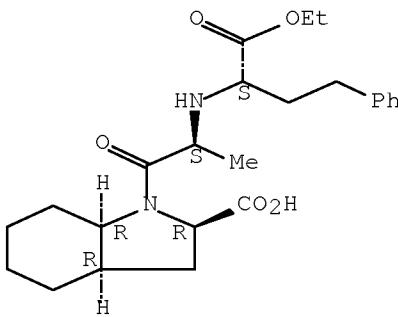
Absolute stereochemistry.



RN 80876-03-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2R-[1[S*(S*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

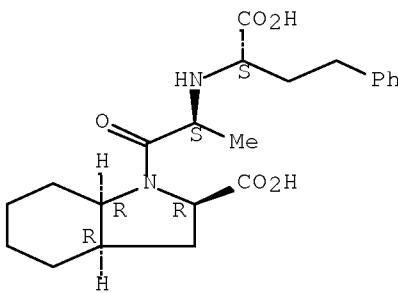


● HCl

RN 80876-05-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2 α ,3 $\alpha\beta$,7 $\alpha\beta$]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



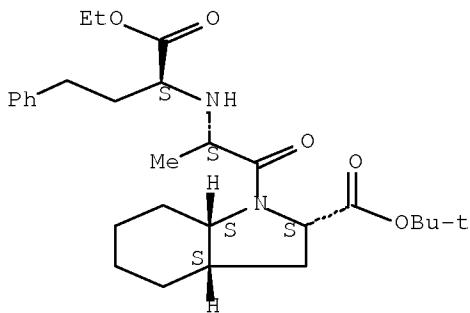
IT 80828-33-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

RN 80828-33-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester,
[2S-[1[R*(R*)],2 α ,3 $\alpha\beta$,7 $\alpha\beta$]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



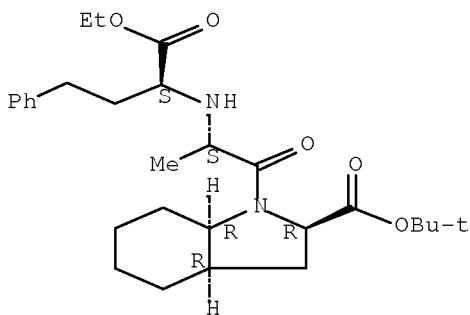
IT 80876-04-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and partial hydrolysis of)

RN 80876-04-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester,
[2R-[1[S*(S*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L36 ANSWER 108 OF 111 CAPLUS COPYRIGHT 2008 ACS

on STN

AN 1982:616730 CAPLUS Full-text

DN 97:216730

OREF 97:36397a, 36400a

TI Carboxyalkyl dipeptides and pharmaceutical compositions containing them

IN Neustadt, Bernard R.; Gold, Elijah H.; Smith, Elizabeth M.

PA Schering Corp., USA

SO Eur. Pat. Appl., 123 pp.

CODEN: EPXXDW

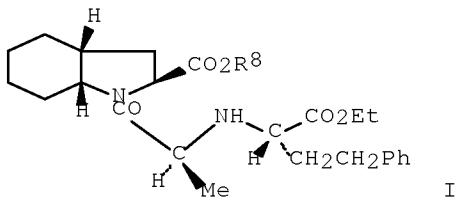
DT Patent

LA English

FAN.CNT 6

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|------------|------|----------|-----------------|----------|
| PI | EP 50800 | A1 | 19820505 | EP 1981-108348 | 19811015 |
| | EP 50800 | B1 | 19860618 | | |

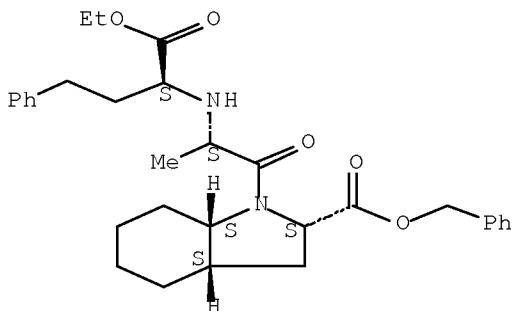
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|---|----|----------|----------------|
| EP 50800 | B2 | 19950607 | |
| R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | |
| AT 20469 | T | 19860715 | AT 1981-108348 |
| DK 8104625 | A | 19820424 | DK 1981-4625 |
| DK 161523 | B | 19910715 | |
| DK 161523 | C | 19911223 | |
| FI 8103283 | A | 19820424 | FI 1981-3283 |
| FI 83222 | B | 19910228 | |
| FI 83222 | C | 19910610 | |
| AU 8176614 | A | 19820429 | AU 1981-76614 |
| AU 554362 | B2 | 19860821 | |
| ZA 8107261 | A | 19820929 | ZA 1981-7261 |
| CA 1341206 | C | 20010320 | CA 1981-388336 |
| NO 8103546 | A | 19820426 | NO 1981-3546 |
| NO 164983 | B | 19900827 | |
| NO 164983 | C | 19901205 | |
| JP 57112359 | A | 19820713 | JP 1981-168511 |
| JP 01032240 | B | 19890629 | |
| IL 64085 | A | 19861231 | IL 1981-64085 |
| HU 32785 | A2 | 19840928 | HU 1981-3078 |
| HU 193146 | B | 19870828 | |
| US 4587258 | A | 19860506 | US 1984-635390 |
| US 4808573 | A | 19890228 | US 1987-29293 |
| US 4818749 | A | 19890404 | US 1987-117008 |
| US 4831157 | A | 19890516 | US 1988-250300 |
| JP 01163197 | A | 19890627 | JP 1988-283542 |
| PRAI US 1980-199886 | A | 19801023 | |
| US 1981-258484 | A | 19810428 | |
| US 1980-201649 | A2 | 19801028 | |
| EP 1981-108348 | A | 19811015 | |
| US 1981-334053 | A2 | 19811223 | |
| US 1984-635390 | A2 | 19840730 | |
| WO 1985-US1406 | A | 19850726 | |
| US 1986-817639 | A3 | 19860110 | |
| US 1987-29293 | A2 | 19870323 | |
| OS MARPAT 97:216730 | | | |
| GI | | | |



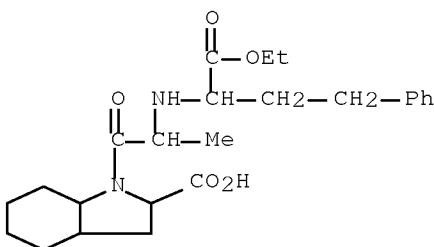
AB RCOCR1R2NHCHR3CONR4CR5R7COR6 [R, R6 = OH, (un)substituted alkoxy, alkenyloxy, (un)substituted NH2; R1 = H, (un)substituted alkyl; R2, R7 = H, (un)substituted alkyl; R3 = H, (un)substituted alkyl, (un)substituted phenylalkyl; R4, R5 = H, (un)substituted alkyl; R4R5 form ring systems] were prepared as antihypertensives and angiotensin-converting enzyme inhibitors (no data). Thus, H-L-Ala-OCH₂Ph tosylate was treated with PhCH₂CH₂COCO₂Et and reduced with NaBH₃(CN) and then debenzylated by hydrogenolysis to give (S)-PhCH₂CH₂CH(CO₂Et)-L-Ala-OH. The latter was condensed with cis,syn-

IT octahydroindole-2(S)-carboxylic acid benzyl ester to give indole I ($R_8 = CH_2Ph$), which was debenzylated by hydrogenolysis to give I ($R_8 = H$).
 83542-05-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and hydrogenolysis of)
 RN 83542-05-6 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,
 $[2S\text{-}[1[R^*(R^*)],2\alpha,3\alpha\beta,7\alpha\beta]]-$ (9CI) (CA INDEX NAME)

Absolute stereochemistry.

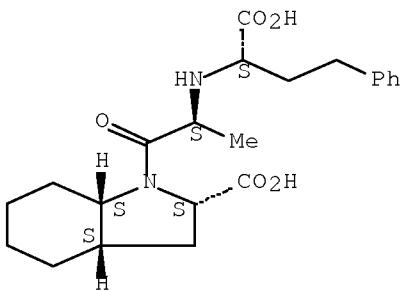


IT 80876-02-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and saponification of)
 RN 80876-02-4 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



IT 80828-34-8P 80876-01-3P 80876-02-4P
 83542-06-7P 83542-08-9P 83601-86-9P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 80828-34-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

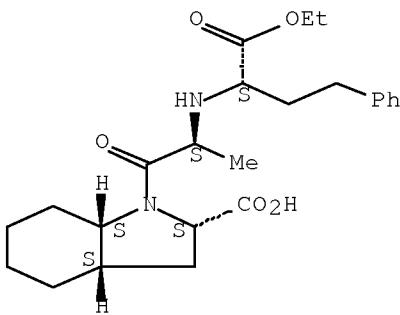
Absolute stereochemistry.



RN 80876-01-3 CAPLUS

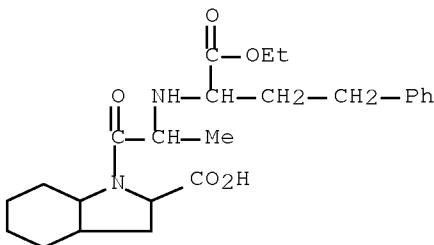
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 80876-02-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)

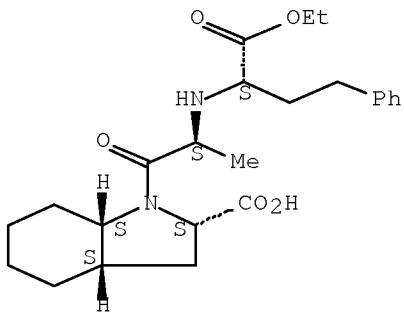


RN 83542-06-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2alpha,3alpha,7alpha]-, monoacetate (9CI) (CA INDEX NAME)

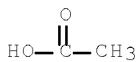
CRN 80876-01-3
CMF C24 H34 N2 O5

Absolute stereochemistry.



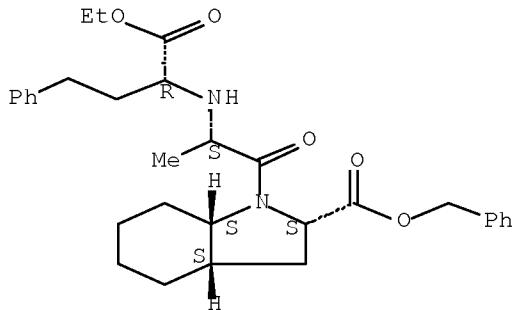
CM 2

CRN 64-19-7
CMF C2 H4 O2

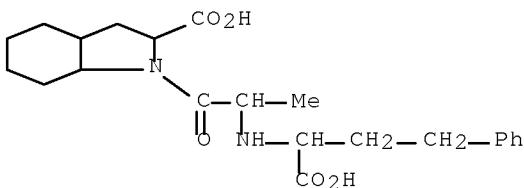


RN 83542-08-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R*(S*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 83601-86-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



L36 ANSWER 109 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1982:616716 CAPLUS Full-text

DN 97:216716

OREF 97:36393a, 36396a

TI Substituted imino diacids and pharmaceutical preparations containing them

IN Remond, Georges; Laubie, Michel; Vincent, Michel

PA Science Union et Cie., Societe Francaise de Recherche Medicale, Fr.

SO Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

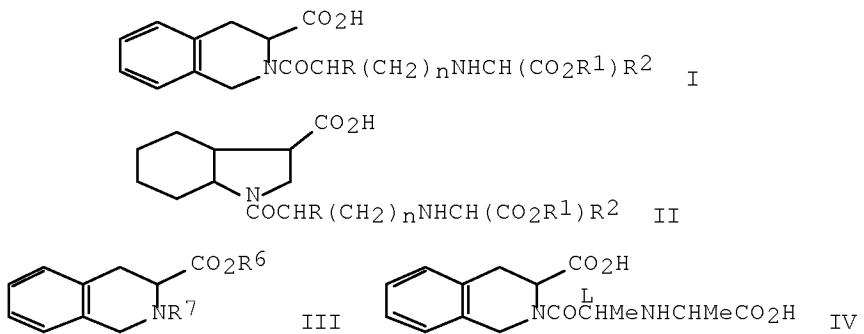
DT Patent

LA French

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | EP 49658 | A1 | 19820414 | EP 1981-401501 | 19810929 |
| | EP 49658 | B1 | 19840613 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| | FR 2491469 | A1 | 19820409 | FR 1980-21095 | 19801002 |
| | FR 2491469 | B1 | 19830513 | | |
| | FR 2503155 | A2 | 19821008 | FR 1981-6916 | 19810407 |
| | FR 2503155 | B2 | 19830701 | | |
| | IL 63940 | A | 19850630 | IL 1981-63940 | 19810925 |
| | AT 7910 | T | 19840615 | AT 1981-401501 | 19810929 |
| | FI 8103034 | A | 19820403 | FI 1981-3034 | 19810930 |
| | FI 77230 | B | 19881031 | | |
| | FI 77230 | C | 19890210 | | |
| | DK 8104343 | A | 19820403 | DK 1981-4343 | 19811001 |
| | DK 157011 | B | 19891030 | | |
| | DK 157011 | C | 19900326 | | |
| | NO 8103339 | A | 19820405 | NO 1981-3339 | 19811001 |
| | NO 160780 | B | 19890220 | | |
| | NO 160780 | C | 19890531 | | |
| | AU 8175949 | A | 19820408 | AU 1981-75949 | 19811001 |
| | AU 542611 | B2 | 19850228 | | |
| | HU 28405 | A2 | 19831228 | HU 1981-2838 | 19811001 |
| | HU 185147 | B | 19841228 | | |
| | SU 1153827 | A3 | 19850430 | SU 1981-3344196 | 19811001 |
| | CA 1341196 | C | 20010306 | CA 1981-387093 | 19811001 |
| | JP 57091974 | A | 19820608 | JP 1981-157367 | 19811002 |
| | JP 01032239 | B | 19890629 | | |
| | ZA 8106844 | A | 19820929 | ZA 1981-6844 | 19811002 |
| | US 4508729 | A | 19850402 | US 1981-308234 | 19811002 |
| | US 4565819 | A | 19860121 | US 1982-420005 | 19820920 |
| | US 4616029 | A | 19861007 | US 1984-659275 | 19841010 |
| | US 4616031 | A | 19861007 | US 1984-659276 | 19841010 |
| | US 4644008 | A | 19870217 | US 1984-659274 | 19841010 |
| | US 4616030 | A | 19861007 | US 1984-679320 | 19841206 |

| | | | | |
|------|----------|-------------|--------|-----------|
| PRAI | FR | 1980-21095 | A | 19801002 |
| | FR | 1981-6916 | A | 19810407 |
| | FR | 1979-30046 | A | 19791207 |
| | FR | 1980-16875 | A | 19800731 |
| | US | 1980-212607 | A2 | 19801203 |
| | EP | 1981-401501 | A | 19810929 |
| | US | 1981-308234 | A1 | 19811002 |
| OS | CASREACT | 97:216716; | MARPAT | 97:216716 |
| GI | | | | |



AB Heterocyclic amino acid derivs. I and II [R = C1-4 alkyl; R1 = H, C1-4 alkyl; R2 = alkyl, mono- or dicycloalkylalkyl, phenylalkyl, $(CH_2)_m X CHR_3 R_4$ [R3 = H, C1-4 alkyl, C3-6 cycloalkyl; R4 = H, C1-4 alkyl, C3-6 cycloalkyl, alkoxy carbonyl; X = S, NR5 (R5 = H, Ac, CO₂CH₂Ph), m = 1, 2]; n = 0, 1] were prepared. Thus, (S)-phenylalanine was cyclized with H₂CO to give (S)-isoquinoline (S)-III (R6 = R7 = H), which was esterified with MeOH/SOC₁₂ and then condensed with Boc-L-Ala-OH (Boc = Me₃CO₂C) by DCC/1-hydroxybenzotriazole to give (S)-III (R6 = Me, R7 = Boc-L-Ala). The latter was saponified and then Boc-deblocked by CF₃CO₂H to give (S)-III.CF₃CO₂H (R6 = H, R7 = H-L-Ala), which was treated with MeCOCO₂H and then reduced by NaBH₃CN to give isoquinoline (2S)-IV. I and II were useful as therapeutic agents due to their ability to inhibit enkephalinase, carboxypolypeptidase, kininase, and angiotensin-converting enzyme (ACE); e.g., the compds. can be used as antihypertensives since they inhibit ACE.

IT 82961-92-OP
RL: SPN (Synthetic preparation); PREP (Preparation)

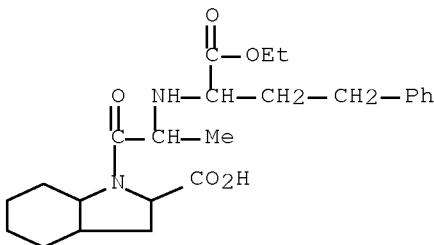
BN 82961-92-0 CAPIUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2Z)-2-butenedioate (2:1) (CA INDEX NAME)

CM 1

CRN 80876-02-4

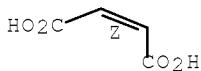
CMF C24 H34 N2 O5



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



L36 ANSWER 110 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1982:492759 CAPLUS [Full-text](#)

DN 97:92759

OREF 97:15483a,15486a

TI Amino acid derivatives, compositions containing them and their use

IN Geiger, Rolf; Teetz, Volker; Urbach, Hansjoerg; Schoelkens, Bernward; Henning, Rainer

PA Hoechst A.-G., Fed. Rep. Ger.

SO Eur. Pat. Appl., 196 pp.

CODEN: EPXXDW

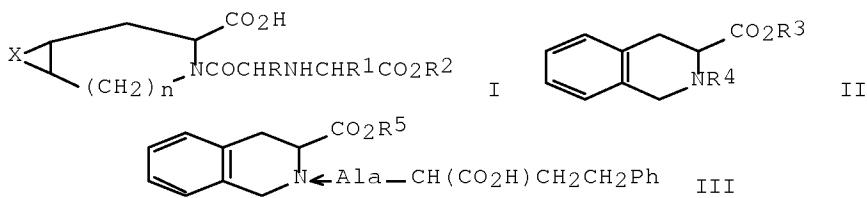
DT Patent

LA German

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | EP 46953 | A2 | 19820310 | EP 1981-106535 | 19810822 |
| | EP 46953 | A3 | 19820505 | | |
| | EP 46953 | B1 | 19891206 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| | DE 3032709 | A1 | 19820429 | DE 1980-3032709 | 19800830 |
| | DE 3118191 | A1 | 19821125 | DE 1981-3118191 | 19810508 |
| | EP 278530 | A2 | 19880817 | EP 1988-102408 | 19810822 |
| | EP 278530 | A3 | 19890802 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | EP 328160 | A1 | 19890816 | EP 1989-105371 | 19810822 |
| | EP 328160 | B1 | 19940504 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| AT | 48415 | T | 19891215 | AT 1981-106535 | 19810822 |
| AT | 105301 | T | 19940515 | AT 1989-105371 | 19810822 |

| | | | | | | |
|------|------------------------------------|----|----------|----|-------------|----------|
| FI | 8102652 | A | 19820301 | FI | 1981-2652 | 19810827 |
| FI | 90072 | B | 19930915 | | | |
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| HU | 27874 | A2 | 19831128 | HU | 1981-2478 | 19810827 |
| HU | 189531 | B | 19860728 | | | |
| DK | 8103835 | A | 19820301 | DK | 1981-3835 | 19810828 |
| DK | 169382 | B1 | 19941017 | | | |
| NO | 8102933 | A | 19820301 | NO | 1981-2933 | 19810828 |
| AU | 8174718 | A | 19820311 | AU | 1981-74718 | 19810828 |
| AU | 544756 | B2 | 19850613 | | | |
| ZA | 8105988 | A | 19820825 | ZA | 1981-5988 | 19810828 |
| IL | 63683 | A | 19880331 | IL | 1981-63683 | 19810828 |
| JP | 01048918 | B | 19891020 | JP | 1981-134401 | 19810828 |
| US | 5158959 | A | 19921027 | US | 1983-565900 | 19831227 |
| US | 5162362 | A | 19921110 | US | 1983-565887 | 19831227 |
| ES | 530715 | A5 | 19850614 | ES | 1984-530715 | 19840316 |
| AU | 8779284 | A | 19880204 | AU | 1987-79284 | 19871001 |
| AU | 599151 | B2 | 19900712 | | | |
| JP | 01125398 | A | 19890517 | JP | 1988-209625 | 19880825 |
| JP | 06078355 | B | 19941005 | | | |
| AU | 8936625 | A | 19891005 | AU | 1989-36625 | 19890620 |
| AU | 627741 | B2 | 19920903 | | | |
| JP | 04217994 | A | 19920807 | JP | 1991-77208 | 19910318 |
| JP | 07121955 | B | 19951225 | | | |
| FI | 90069 | B | 19930915 | FI | 1991-4555 | 19910927 |
| FI | 90069 | C | 19931227 | | | |
| FI | 90532 | B | 19931115 | FI | 1991-4554 | 19910927 |
| FI | 90532 | C | 19940225 | | | |
| US | 5401766 | A | 19950328 | US | 1994-208443 | 19940309 |
| PRAI | DE 1980-3032709 | A | 19800830 | | | |
| | DE 1981-3118191 | A | 19810508 | | | |
| | EP 1981-106535 | P | 19810822 | | | |
| | EP 1989-105371 | A | 19810822 | | | |
| | US 1981-297191 | A3 | 19810828 | | | |
| | JP 1982-117311 | A | 19820705 | | | |
| | JP 1982-117312 | A | 19820705 | | | |
| OS | CASREACT 97:92759; MARPAT 97:92759 | | | | | |
| GI | | | | | | |



AB Amino acid derivs. I (X = fused benzene or cyclohexane ring; R, R1 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl, aryl, partially hydrogenated aryl, aralkyl, heterocyclic residue; R2 = H, alkyl, alkenyl, aralkyl; n= 0, 1) were prepared as long-lasting antihypertensives (no data). Thus, tetrahydroisoquinoline II (R3 = R4 = H) was treated with ZCl (Z = PhCH2O2C) to give II (R3 = H, R4 = Z), which was esterified with Me3COH by DCC in CH2C12 containing 4-(dimethylamino)pyridine to give 97% II (R3 = CMe3, R4 =

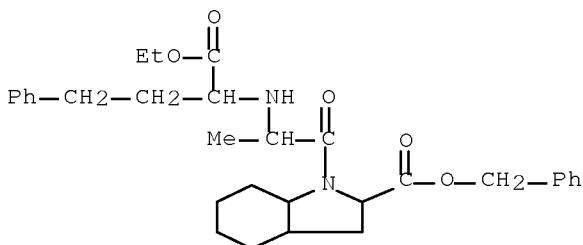
Z), which was Z-deblocked by hydrogenolysis and then condensed with Z-Ala-OH by DCC/1-hydroxybenzotriazole to give II (R₃ = CMe₃, R₄ = Z-Ala). The latter was Z-deblocked by hydrogenolysis to give II (R = CMe₃, R₄ = Ala), which was condensed with PhCH₂CH₂COCO₂H and was then reduced with NaBH₃CN to give isoquinoline III (R₅ = CMe₃), which was debutylated by CF₃CO₂H to give III (R₅ = H).

IT 82717-98-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

RN 82717-98-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester (CA INDEX NAME)

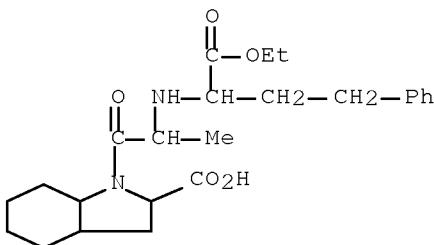


IT 80876-02-4P 82717-98-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

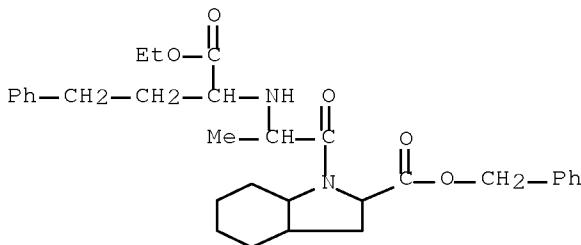
RN 80876-02-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



RN 82717-98-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester (CA INDEX NAME)



**L36 ANSWER 111 OF 111 CAPLUS COPYRIGHT 2008 ACS
on STN**

AN 1982:122630 CAPLUS Full-text

DN 96:122630

OREF 96:20133a, 20136a

TI Substituted acyl derivatives of octahydro-1H-indole-2-carboxylic acids

IN Hoefle, Milton Louis; Bobowski, George

PA Warner-Lambert Co., USA

SO Eur. Pat. Appl., 47 pp.

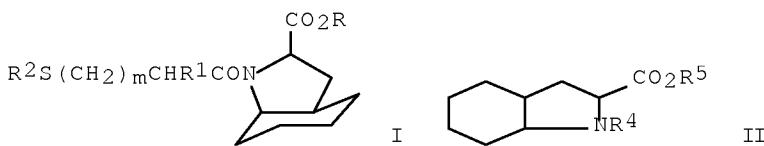
CODEN: EPXXDW

DT Patent

LA English

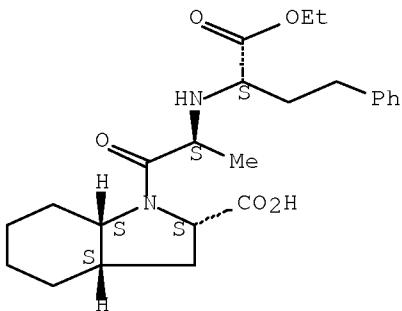
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | EP 37231 | A2 | 19811007 | EP 1981-301243 | 19810324 |
| | EP 37231 | A3 | 19820428 | | |
| | EP 37231 | B1 | 19870128 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| | US 4350704 | A | 19820921 | US 1981-233940 | 19810217 |
| | ZA 8101493 | A | 19820331 | ZA 1981-1493 | 19810305 |
| | EP 88341 | A1 | 19830914 | EP 1983-101990 | 19810324 |
| | EP 88341 | B1 | 19870722 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | EP 88342 | A1 | 19830914 | EP 1983-101991 | 19810324 |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | AT 25243 | T | 19870215 | AT 1981-301243 | 19810324 |
| | AU 8168939 | A | 19811008 | AU 1981-68939 | 19810331 |
| | AU 543861 | B2 | 19850509 | | |
| | SU 1246893 | A3 | 19860723 | SU 1981-3339202 | 19811005 |
| | SU 1241988 | A3 | 19860630 | SU 1982-3498497 | 19821010 |
| PRAI | US 1980-137106 | A | 19800402 | | |
| | US 1980-194307 | A | 19801006 | | |
| | US 1981-233940 | A | 19810217 | | |
| | EP 1981-301243 | P | 19810324 | | |
| OS | MARPAT 96:122630 | | | | |
| GI | | | | | |



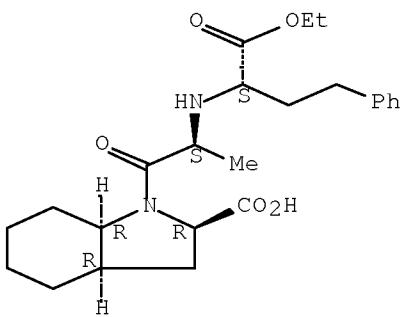
- AB Indolecarboxylates I [R = H, alkyl; R1 = H, alkyl, CH2Ph; R2 = H, COR3 (R3 = alkyl, C4-9N1-2O1-2S1-2 heteroaryl, Ph optionally substituted with 1 or 2 F, Cl, Br, alkyl, alkoxy); n = 0, 1], useful antihypertensives, were prepared. Et indole-2-carboxylate was hydrogenated and the octahydro ester 2 α ,3 $\alpha\beta$,7 $\alpha\beta$ -II (R4 = H, R5 = Et) hydrolyzed to give 2 α ,3 $\alpha\beta$,7 $\alpha\beta$ -II (R4 = R5 = H).HCl. N-Acylation this in pyridine with AcSCH2CHMeCOCl gave 2 α ,3 $\alpha\beta$,7 $\alpha\beta$ -II (R4 = COCHMeCH2SAc, R5 = H) diastereoisomer A which was hydrolyzed with NH3 in MeOH to give 2 α ,3 $\alpha\beta$,7 $\alpha\beta$ -II (R4 = COCHMeCH2SH, R5 = H) diastereoisomer A, which had in vitro IC50 (inhibitory concentration) for angiotensin converting enzyme of 7.0 + 10⁻⁹ M.
- IT 80876-01-3 80923-95-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(angiotensin converting enzyme inhibitory activity of)
- RN 80876-01-3 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



- RN 80923-95-1 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2 α ,3 $\alpha\beta$,7 $\alpha\beta$]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 80828-34-8P 80876-05-7P

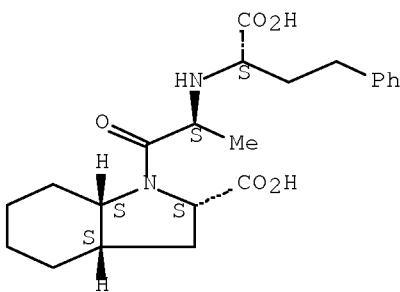
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and angiotensin converting enzyme inhibitory activity of)

RN 80828-34-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

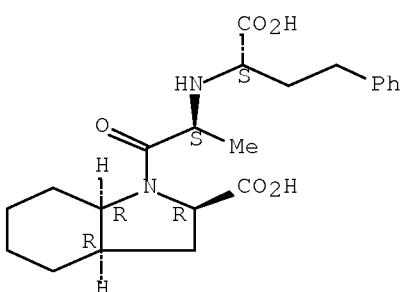
Absolute stereochemistry.



RN 80876-05-7 CAPLUS

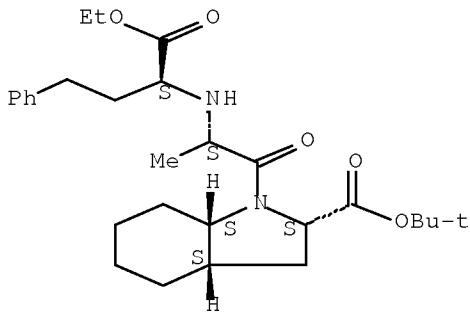
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2α,3αβ,7αβ]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



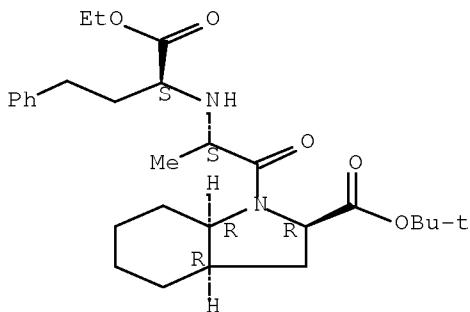
IT 80828-33-7P 80876-04-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and hydrolysis of)
 RN 80828-33-7 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester,
 [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

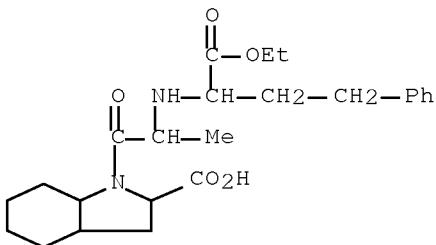


RN 80876-04-6 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester,
 [2R-[1[S*(S*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 80876-02-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 80876-02-4 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)



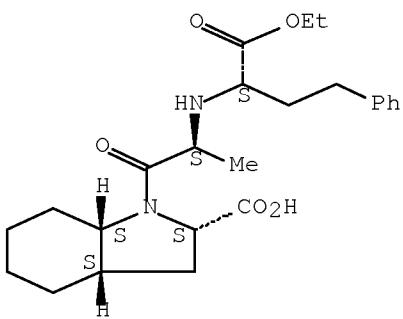
IT 80828-32-6P 80876-03-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, saponification and hydrolysis of)

RN 80828-32-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[1S]-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1),
(2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

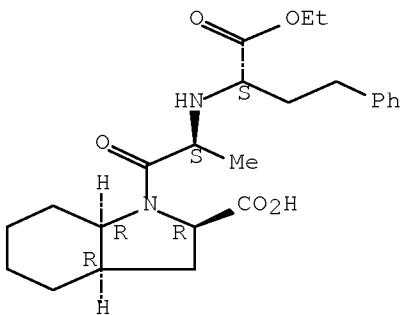


● HCl

RN 80876-03-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride,
[2R-[1[S*(S*)],2a,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

=> log hold

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

605.91

1621.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-88.80

-112.80

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 10:58:51 ON 05 MAY 2008